Virtual reality based kinematics for assessment of post-stroke upper limb function

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Gothenburg 2020

Cover illustration: Trajectories of arm movement of individuals at month 6 after stroke. Illustration by Netha Hussain.

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ISBN 978-91-7833-826-9 (PRINT)
ISBN 978-91-7833-827-6 (PDF)

Printed in Gothenburg, Sweden 2020
Printed by Stema Specialtryck AB

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Truth alone triumphs

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Abstract

Stroke is a leading cause of disability in adults and upper limb impairment is one of the most common functional limitations in individuals after stroke. Stroke recovery of the upper limb has been sparsely assessed using kinematic methods coupled with the virtual reality technique, despite its availability for stroke rehabilitation. There is little data regarding the relationship between objectively assessed arm function and self-perceived manual ability in individuals after stroke.

The overall aim of this thesis was to develop a method for assessing the upper limb sensorimotor function following stroke using virtual reality-based technique. The specific aims were to determine discriminant validity, concurrent validity and longitudinal change of kinematic variables, along with establishing the relationship of self-perceived manual ability with kinematic variables from day 3 to month 12 after stroke.

Methods: The studies reported in this thesis included 67 individuals extracted from the SALGOT (Stroke Arm Longitudinal Study at the University of Gothenburg) cohort and 43 healthy controls. They performed the target-to-target pointing task in a virtual environment using a haptic stylus that captured kinematic parameters. The main clinical outcome measures used for these studies were: Fugl-Meyer Assessment for Upper Extremity (FMA-UE), Action Research Arm Test (ARAT) and ABILHAND questionnaire.

Results: The kinematic variables of movement time, mean velocity, peak velocity and number of velocity peaks were discriminative for groups with moderate to mild stroke impairment, as well as healthy controls. Mean velocity and number of velocity peaks together explained 16% of the FMA-UE score, while movement time and number of velocity peaks explained 13% and 10% of ARAT score respectively. Movement time, mean velocity and number of velocity peaks showed improvement over time and were affected positively by younger age, less severe stroke and ischemic compared to hemorrhagic stroke. Except for the measurement at 6 months, movement time and number of velocity peaks differed significantly from that of healthy controls within one year after stroke. The correlation between self-reported manual ability and kinematic variables were low or very low early after stroke, which became moderate to high after 6 months for movement time and number of velocity peaks, but remained low to moderate for mean velocity and low for peak velocity.

Conclusions and clinical implications: The end-point kinematic variables, particularly movement time and number of velocity peaks were demonstrated to be most effective in characterizing the upper extremity function and for capturing the improvement over time after stroke. This knowledge is useful in movement analysis research, especially in the development of new virtual reality-based devices. As there is a discrepancy between self-reported and objectively assessed arm function especially in the acute stage of stroke, a combination of self-reported and objective assessments of the upper limb should be used as outcome measures for gathering full understanding of the individual's functional level and for setting achievable rehabilitation goals.

Keywords: stroke, virtual reality, kinematics, upper extremity

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ISBN 978-91-7833-827-6 (PDF)
http://hdl.handle.net/2077/63288

Populärvetenskaplig sammanfattning

Stroke är ett tillstånd där blodtillförseln minskar till delar av hjärnan, antingen på grund av en blodpropp eller på grund av en blödning vilket leder till en hjärnskada. Det gör att efter en stroke är det vanligt att individer upplever nedsatt förmåga att kommunicera, komma ihåg saker, röra sig eller ha nedsatt känsel. Omkring 50-80% av de som drabbats av stroke uppvisar funktionsnedsättning i armarna. Dessa funktionsnedsättningar kommer i sin tur att påverka personens förmåga att delta i sina dagliga aktiviteter. Eftersom miljontals personer runt om i världen lever med följderna av stroke, är det viktigt att forska om funktionen i övre extremitet efter stroke.

I denna avhandling låg fokus på att skapa en ny metod för att mäta armfunktion hos personer efter stroke. Armrörelserna mättes med en enkel, datorbaserad arbetsuppgift som använder virtual reality, en teknik som används i 3D-filmer. I denna uppgift använde deltagarna en pennliknande enhet för att peka och trycka på virtuella föremål placerade framför kroppen. Enheten registrerade rörelser tid och rum i tre dimensioner. Rörelsedata bearbetades och omförhandlades till matematiska komponenter, så kallade kinematiska mått, som användes för att studera rörelsemönster. För de fyra studier som finns i denna avhandling samlades data in från 67 personer med stroke och 43 friska personer.

Studie I syftade till att ta reda på skillnader i rörelsemönster hos personer med mild och måttlig nedsättning av armfunktion efter stroke jämfört med friska personer. Studien visade att kinematiska mått såsom rörelsetid, medelhastighet, maxhastighet och rörelsesmidighet var annorlunda hos personer med nedsatt armfunktion vid stroke jämfört med friska personer. Denna information är möjlig att använda för planering av behandling av personer med stroke.

Studie II syftade till att ta reda på hur väl de kinematiska måtten är relaterade till kliniska bedömningsinstrument. Två bedömningsinstrument användes, en som bedömer funktionsnedsättning (Fugl-Meyer bedömning av sensomotorisk funktion av övre extremitet) och en som bedömer aktivitetsförmåga (Action Research Arm Test). Resultaten visade att nedsatt armfunktion kan i viss grad (16%) förklaras med kinematiska mått på medelhastighet och rörelsesmidighet. Aktivitetsförmåga kan i viss utsträckning (10-13%) förklaras med rörelsetid och rörelsesmidighet. Detta betyder att kinematiska mått och kliniska bedömningsinstrument verkar avspegla lite olika aspekter av armrörelser hos personer med stroke. Därför bör information från båda inkluderas vid utvärdering av nedsatt rörelseförmåga hos personer med stroke.

Studie III syftade till att ta reda på hur återhämtningen av armfunktionen efter stroke visar sig genom en förändring av de kinematiska måtten mellan 3 dagar och 12 månader efter stroke. Resultaten visade att rörelsetid, medelhastighet och smidighet förbättras med tiden. Resultaten visade också att armfunktion kan förbättras även efter tre månader efter stroke. Rörelsetid och smidighet nådde nästan normala nivåer 6 månader efter stroke, men försämrades igen vid 12 månader. Förbättringen var större hos yngre personer, som hade mindre allvarliga stroke och som hade en stroke orsakad av en blodpropp och inte en blödning. Resultaten tyder på att personer med stroke kan ha svårt att vidmakthålla sin armfunktion sent efter sin stroke. Därför kan de behöva fortsatt hjälp från sjukvården för att uppnå optimal förbättring och för att förhindra försämring.

Studie IV syftade till att ta reda på hur den självrapporterade manuella förmågan hos personer med stroke är relaterad till objektiva kinematiska mått. Resultaten visade att styrkan i sambandet mellan självrapporterade och objektiva mätningar var lägre tidigt efter stroke och ökade med tiden fram till 12 månader efter stroke. Våra resultat visar på att det kan vara svårt för individer att förstå och tolka hur de nya funktionsnedsättningarna påverkar deras aktiviteter i det dagliga livet tidigt efter stroke. Man bör ta hänsyn till denna aspekt när den manuella förmågan bedöms efter stroke. Uppgifter från självskattningsinstrument är användbara både för personer med stroke och kliniker för att kunna sätta realistiska rehabiliteringsmål.

Ytterligare forskning som analyserar armens rörelseförmågan och -kvalitet i olika aktiviteter behövs för att förstå de underliggande mekanismerna vid återhämtning efter stroke. Resultaten från denna avhandling är användbar när nya utvärderings- och rehabiliteringsmetoder utvecklas.

Popular Science Summary

Stroke is a condition where blood supply carrying nutrients and oxygen gets reduced to a focal part of the brain, either due to a clot or due to bleeding. After stroke, it is common for individuals to experience reduced ability to communicate, remember things or move or sense one side of the body. Approximately 50-80% of individuals after stroke have impairments of the upper limb. These impairments will in turn affect the person's ability to take part in her or his daily-life activities. As millions of people around the world live with the aftereffects of stroke, it is important to conduct research about their upper limb function after stroke.

In this thesis, the focus was on creating a new method for measuring the arm function of people with stroke. The arm movements were measured with a simple, computer-based task that uses virtual reality, a technology used in 3D movies. In this task, the participants used a pen-like device to point at virtual targets placed in front of the arms' working space. This device registered the participants' time and route of movement in the 3D space. This movement data was stored in a computer and extracted into mathematical components, called kinematic measures, which were useful for studying the movement patterns. For the four studies present in this thesis, data from 67 people with stroke and 43 healthy people were taken.

Study I aimed to find out the differences in movement patterns between people with mild and moderate arm impairment after stroke and healthy people. In this study, kinematic measures like movement time, average speed, peak speed and movement smoothness were found to be different in people with various levels of arm impairment in stroke when compared to healthy people. This information is useful for planning the treatment of people with stroke.

Study II aimed to find out how well the kinematic measures are related to the clinical scales commonly used for assessing arm impairment. Two assessment scales, one assessing impairment (Fugl-Meyer Assessment of Upper Extremity) and one assessing activity capacity (Action Research Arm Test) were used. The results showed that arm impairment to some degree (16%) could be explained by the kinematic measures of average speed and smoothness. Activity capacity could be explained to some degree (10-13%) by movement time and smoothness measures. This means that kinematic measures and clinical scales seem to measure somewhat different aspects of arm movement in people with stroke. Therefore, information from both should be considered while evaluating movement deficits in people with stroke.

Study III aimed to find out how the recovery of arm function after stroke occurs in terms of improvement in kinematic measures between 3 days and 12 months after stroke. The results showed that movement time, average speed and smoothness get better with time. This improvement is increased further in people who are younger, who have less severe stroke and who had a stroke caused by a clot and not a bleeding. The results also showed that the arm function could improve even beyond 3 months after stroke. Movement time and smoothness reached almost normal levels at 6 months after stroke, but decreased again at 12 months. This indicates that people with stroke can have difficulty in retaining their arm function at later stages of stroke and that they might need some help from the healthcare system in order to continue to recover and to prevent their arm function from becoming worse.

Study IV aimed at finding out how the self-reported manual ability of people with stroke is related to objective kinematic measures. The results showed that the strength of relationship between self-reported and objective measurements was lower early after stroke and increased with time until 12 months after stroke. Our results indicate that in the early stages of stroke, it can be difficult for individuals to fully perceive and interpret how the new deficits can impact their activities of daily life. This aspect should be considered while the manual ability is assessed after stroke. Furthermore, information from self-reported scales is useful for people with stroke and for clinicians in order to set realistic rehabilitation goals.

Further research using analysis of movement performance and quality in different upper limb tasks is needed to understand the underlying mechanisms of recovery after stroke. Knowledge from this thesis is useful when new assessment and rehabilitation methods are developed.

List of papers

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Hussain N, Alt Murphy M, Sunnerhagen KS. Upper limb kinematics in stroke and healthy controls using target-to-target task in virtual reality. *Frontiers in Neurology*. 2018;9:300

II. Hussain N, Sunnerhagen KS, Alt Murphy M. End-point kinematics using virtual reality explaining upper limb impairment and activity capacity in stroke. *Journal of Neuroengineering and Rehabilitation*. 2019;16(1):82

III. Hussain N, Sunnerhagen KS, Alt Murphy M. Recovery of arm function from acute to chronic stage of stroke quantified by kinematics (Submitted manuscript)

IV. Hussain N, Alt Murphy M, Lundgren-Nilsson Å. Sunnerhagen KS. Relationship between self-reported and objectively measured manual ability varies during the first year post-stroke. *Scientific Reports*. 2020;10(1):5093

Contents

Introduction

Stroke

Stroke is a non-communicable disease that is caused due to the interruption of blood flow to parts of the brain, causing sudden death of brain cells. Stroke is defined by the World Health Organization (WHO) as “rapidly developing clinical signs of focal (or global, in case of deep coma) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin” (1, 2). Based on the mechanism of interruption to the blood flow, stroke is classified into ischemic stroke and haemorrhagic stroke, with haemorrhagic stroke being further classified into intracerebral haemorrhage and subarachnoid haemorrhage depending on the site of bleeding. Ischemic stroke is caused by focal infarction to the brain secondary to interrupted blood flow, while intracerebral haemorrhagic stroke results from a focal collection of blood in the brain parenchyma or ventricles. Stroke due to subarachnoid haemorrhage is a consequence of bleeding into the subarachnoid space in the absence of trauma (3). The worldwide incidence of ischemic stroke is twice as much as haemorrhagic stroke (4).

The global lifetime risk of stroke is 25% from the age of 25 years onward (5). Stroke is a leading cause for disability in adults (6), accounting for 102 million Disability Adjusted Life Years (DALY) lost in a total of 33 million individuals globally (4). Approximately 22,000 individuals in Sweden and 1 million individuals in India suffer from stroke in a year (7, 8). Globally, 90% of the burden of stroke was attributable to modifiable risk factors such as high blood pressure, poor diet and smoking (9). Although stroke mortality is decreasing worldwide, the global stroke burden is increasing because of the expanding population numbers and an ageing population (4, 10). The rising levels of two risk factors, obesity and diabetes, play an important role in increasing stroke morbidity and mortality (11).

The physical impairment that follows stroke is heterogeneous and varies with the region of the brain that has sustained the stroke. Individuals with stroke may have various symptoms and sequelae, including impairments in sensation, cognition, movements and perception. As a result, individuals after stroke may face difficulties in mobility, communication, social functioning and occupation in addition to being physically dependent on others (12, 13). Thus, stroke has immense impact not only for the individual, but also for their family, caregivers and the healthcare system, including substantial socio-economic impact.

Arm function after stroke

The upper limb is used for several day-to-day tasks such as pointing, reaching, grasping, gripping and manipulating objects. The human upper limb can perform isolated and coordinated movements as a result of which performing several complex activities is made possible. The main end-effector of the upper limb is the hand, while the wrist, elbow, shoulder and trunk help to place the hand in space (14). The control of upper limb movements is affected by the task, object and the environment (15).

In stroke, the prevalence of upper limb motor impairment is approximately 50-80% in the acute stage (16-18) and 40-50% in the chronic stage (17, 19). Some degree of motor recovery is shown by 65% of the individuals hospitalized after stroke, while complete motor recovery occurs in less than 15% of the individuals (20). In stroke, the arm that is more affected is contralateral to the affected side of the brain. However, the ipsilateral arm might also have impairments to a lesser degree (21-24). The common upper limb impairments after stroke are paresis, abnormal muscle tone and somatosensory changes (25).

Upper limb impairment after stroke results in activity limitation. Therefore, individuals after stroke may experience limitations in performing daily-life tasks. These functional limitations lead on to difficulties in several day-to-day activities such as feeding, dressing, bathing and driving. Individuals with stroke also report self-perceived limitation of arm function (26-28). Arm function can be perceived as limited, even with good observed function of the more-affected limb (26, 28, 29). Accurate assessment of both self-perceived and objective arm function is crucial in understanding the limitations faced by individuals with stroke, devising rehabilitation strategies and developing technology-based devices for rehabilitation.

Stroke Rehabilitation

Rehabilitation is defined as "a set of measures that assist individuals who experience, or are likely to experience disability, to achieve and maintain optimal functioning in interaction with their environments (30). Rehabilitation comprises of a large array of interventions in the biomedical, psychological, social, educational and vocational domain, which can be implemented in institutional or community-based settings (31).

Stroke rehabilitation involves the cyclical process of assessment (identification and quantification of the needs of the individual), goal setting (defining realistic goals for improvement) , intervention (assist the achievement of goals) and re-assessment (assess the progress towards goals) (13). Post-stroke care delivery in a stroke unit and by a multidisciplinary team has been found to be effective for stroke rehabilitation (32, 33). A stroke unit is a designated unit exclusively for individuals after stroke where acute stroke care is provided by multidisciplinary staff. The stroke unit is involved in structured assessments of impairments, early mobilization and rehabilitation (33). Individuals who received organized stroke care, such as in a stroke unit, are likely to survive the stroke, return home and regain independence compared to those who received less-organized service (33).

Rehabilitation of the upper limb is of great importance in stroke rehabilitation (34). Interventions such as task specific training, constraint-induced movement therapy, robot assisted training, virtual reality, mental practice with motor imagery and relatively high doses of repetitive task practice were found to be beneficial for rehabilitation of upper limb after stroke (13, 35, 36). Evidence-based physiotherapy and occupational therapy were also found to be effective for reducing post-stroke impairment of the upper limb (37, 38).

The ICD and ICF frameworks

The International Classification of Diseases (ICD) is the global standard for diagnostic health information (39). At the time of conception of this thesis, the 10th edition of ICD was in use, where stroke was classified under diseases of the circulatory system, and the diagnosis codes I61(intracerebral hemorrhage) and I63 (cerebral infarction) were applicable for the cohort of this thesis (40). In the 11th edition of ICD released in 2018, stroke was classified as a disease of the nervous system, and now the diagnosis codes 8B00.Z (intracerebral hemorrhage) and 8B11 (cerebral ischemic stroke) apply to the cohort of this thesis.

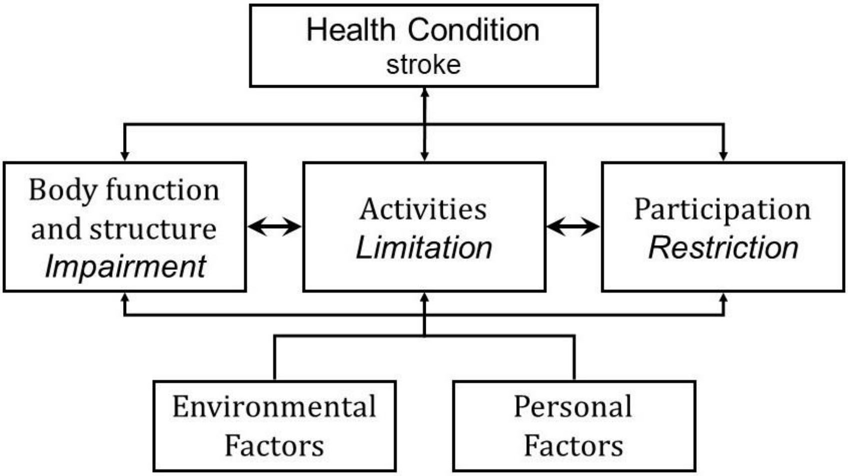

Figure 1. The ICF model showing the interaction of various components

The diagnosis alone cannot explain a person's level of functioning and disability. Hence, the International Classification of Functioning, Disability and Health (ICF) was introduced by World Health Organization for eliciting and recording information on the functioning and disability of an individual (41). The ICF provides a universal, comprehensive and internationally accepted terminology for describing the functioning of an individual. It can be used for capturing, collecting and summarizing various aspects related to stroke in clinical and research context. Thus, it provides a comprehensive description of a person's individual functioning profile, in turn helping to better understand the person's specific needs (41). The 'functioning and disability' components of the ICF are: Body functions and structures, Activities and Participation (Figure 1). The contextual factors are environmental and personal factors, both of which may have an influence on all three 'functioning and disability' components.

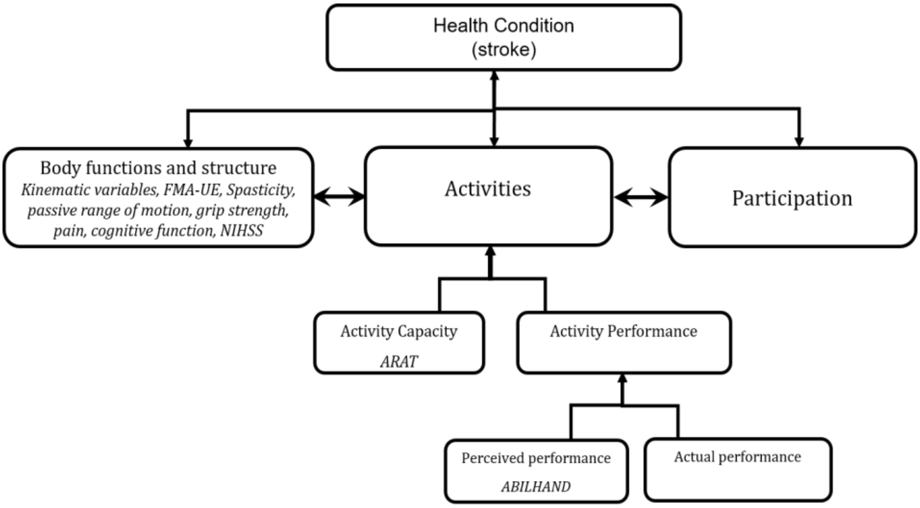

Figure 2: The outcome measures used in this thesis, classified according to ICF.

Performance and capacity are two constructs that can be used as qualifiers in indicating how the environment impacts a person's activities and participation. According to the ICF, capacity relates to what an individual can do in a standardized environment while performance relates to what the person actually does in her or his current environment (41). The gap between capacity and performance reflects the difference between the impacts of current and uniform environments (42). The outcome measures used in this thesis, classified according to ICF are shown in Figure 2.

Recovery after stroke

The motor recovery after stroke occurs in a non-linear pattern. The highest improvement occurs within the first four weeks after stroke, with continued recovery happening mainly until three months after stroke (20, 43, 44). Arm recovery continues to occur even after three-months post-stroke, but to a much lesser degree (43). Sixty-eight percent of individuals with stroke indicate that they have incomplete recovery at 3 months post-stroke, and 71% report not attaining full recovery at 12 months after stroke (12).

There is a wide variation in individual stroke recovery curves of the upper limb between individuals (45), possibly because several factors affect stroke recovery simultaneously. However, some factors are commonly found to affect stroke recovery in a significant way. There is a strong relationship between initial grade of paresis and the functional recovery after stroke, with better recovery occurring in those with lower initial grade of paresis (20, 46, 47). Individuals with hemorrhagic stroke have higher initial arm impairment, but at three months after stroke, there is no difference in their arm function compared to those with ischemic stroke (48, 49). Those with affected dominant arm are more likely to gain better hand strength and lower muscle tone than those with more-affected non-dominant arm (50). Females are less likely to achieve functional independence and have poorer quality of life than males at least until 3 months after stroke (51).

Evidence from animal studies show that number of pre-injury and post-injury factors can affect the recovery after brain injury. Pre-injury exercise and environmental enrichment (such as stimulating physical and social surroundings) protects the animal from damaging effects of brain injury (15). Post-injury factors that affect recovery of function are: pharmacological treatments (which reduce the nervous system’s reaction to injury and promote recovery of function), neurotrophic factors (such as insulin-like growth factor), post-injury exercise and training (15).

Assessment of arm function following stroke

The assessment of upper limb function is central in rehabilitation research and clinical practice for determining the prognosis, planning the course of treatment and evaluating the treatment effects following stroke (52, 53). Conventionally, the assessment of motor function after stroke is performed using standardized clinical scales that measure body function and activity as per the International Classification of Functioning, Disability and Health (ICF) (41).

Clinical scales are the most frequently used assessment methods for post-stroke arm function in research and clinical settings (54). The Fugl-Meyer Assessment of Upper Extremity (FMA-UE), a clinical scale for assessing post-stroke arm function is the most popular scale for assessment of arm function after stroke, with 36% of intervention studies reporting its use between 2004 and 2015 (54). The popularity of the FMA-UE is probably because of its excellent psychometric properties (55), non-reliance on special equipment and long legacy of use in clinical trials. However, as most clinical scales are observer-based, ordinal instruments, they lack the sensitivity to measure subtle sensorimotor deficits in stroke. They are affected by observer bias as well as floor and ceiling effects (56). The limitations of observer-based scales were overcome by introducing techniques for objective measurement of arm function. Some devices such as hand dynamometers have been in use for long time for objective measurement of grip strength, while newer techniques measuring motor performance, such as kinematic analysis, have been introduced more recently.

Kinematic assessment of upper limb

Kinematics is the study of motion of objects, without reference to the forces involved (57). Kinematic analysis involves measuring the kinematic quantities that describe the motion of objects. The popularity of kinematics as an outcome measure after stroke is growing, with 13% of the studies between 2004 and 2015 reporting its use (54). There is also an increasing trend of use of kinematic analysis in combination with FMA-UE as outcome measures in research studies (54). Kinematic analysis allows for sensitive measurements, eliminates observer bias and does not have ceiling effect. Ipsilateral impairments in stroke, which are generally subtle and often difficult to detect using traditional clinical assessments, can be assessed using kinematic analysis (21-24).

The outcome of kinematic analysis is captured as kinematic variables either in two or three dimensions. Some of the commonly used kinematic variables are metrics related to time, velocity and movement smoothness (58). Dozens of kinematic variables are described in literature, which are useful in capturing various aspects of stroke impairment (59-61).

Kinematic assessment of the upper limb can be performed using several methods. Motion capture systems (60) inertial measurement units (IMUs) (62) and robotic devices (63) are the three different methods presently in use for the kinematic assessment of upper limb after stroke. Motion capture can be done using optoelectronic cameras, electromagnetic or ultrasound based devices (60). Optoelectronic system includes a set of high-speed cameras (usually 3-6, but systems with 16 cameras are often used for gait analysis) which can track the position of markers placed on a subject's body using infrared light pulses. Markers attached on the body segments are captured simultaneously and tracked by multiple cameras providing three-dimensional movement data. A set of kinematic variables, such as movement time, speed and acceleration can be calculated from this data. Since several markers are used, the movements of markers relative to each other can also be captured. This provides a possibility to measure joint angles and angular velocities as well. Tasks such as reach-to-grasp, reach-to-target and pointing have all been studied using motion capture systems (60).

Inertial measurement units (IMU) comprise of accelerometers and gyroscopes and is used for motion tracking and analysis. They can be integrated into wearable devices, and hence useful for continuous monitoring of an individual's activities outside lab settings (64). Currently, IMUs are recommended to be used only in conjunction with a camera-based system because of insufficient research around its usefulness (65).

Robotic devices can be broadly classified as exoskeletons or end-effector devices, even though it is not possible to make a strict demarcation between the two types (66). Robotic exoskeletons involve using electronic, computerized control systems to assist arm movements. In addition to kinematic assessment (61), robotic exoskeletons have been used for rehabilitation (67). Exoskeletons vary based on the level of influence exerted by them. Influence refers to the interaction between the individuals and the measurement system that influences the natural free movements, such as the weight of the device and maneuverability. An ideal exoskeleton should have minimal influence in order to be used for assessing natural movements. Pointing, drawing shapes and reach-to-grasp are some of the tasks that have been studied using robotic exoskeletons in individuals with stroke (61). Depending on the maneuverability of the device, the task is performed in 2D or 3D. Robotics allows for capturing kinematic parameters related to time, speed, movement planning, inter-limb coordination, range, smoothness and accuracy (59).

In end-effector devices, movements are generated from the most distal segment of the extremity, and no alignment is required between the joints of the person and the robot (66). They exert minimal influence compared to exoskeletons, and therefore, free arm movements within a pre-defined working space can be performed using this setup. Kinematic data is captured when the individual moves the end-effector by holding it in their hands. Therefore, the dynamic interaction between the components of the upper limb and trunk cannot be captured using this method. On the other hand, end-effector devices are relatively inexpensive, easy to set-up and use compared to optoelectronic cameras and robotic exoskeletons. Thus, end-effectors find application in the assessment and rehabilitation of arm function in conditions such as stroke (68), multiple sclerosis (69) and cerebral palsy (70).

Reaching and pointing movements

Reaching and pointing are two common goal-directed tasks performed using upper limb. Reaching involves moving the arm away from the body in a specified direction with the aim to point or grasp something. Pointing involves reaching out with the arm in order to point or touch something with a finger or a hand. Reaching and pointing are used in daily life activities such as pushing a button, interacting with a touch screen and pressing an electric switch.

The two mechanisms that control movements such as reaching and pointing are feedback control and feedforward control. Feedback control occurs in response to sensory feedback from visual, vestibular and somatosensory organs (15). In feedback control, sensory input of the position of the arm is compared to the desired position of the arm. The difference between the sensory input and the desired state is used to activate the arm muscles and update the movement of the arm. On the other hand, feedforward, or anticipatory control refers to postural responses which are made in anticipation of voluntary movement (15). It involves continuous updating of information from prior experience to activate the muscles to the correct level for achieving the desired output. In the pointing task used in this study, feedforward control likely governs the first visually triggered outward movement, and feedback control is responsible for the later part of the movement where more precision is needed for touching the target.

In healthy individuals, the velocity profile of a goal-directed reaching or pointing task is bell-shaped, with one predominant peak that contains two main phases: the acceleration phase and the deceleration phase (Figure 3). The acceleration phase is the visually triggered outward movement which brings the hand to the vicinity of the target. This is followed by a slower deceleration phase, where the remaining distance towards the target is covered under visual regulation (71). Most of the distance towards the goal is covered during these two phases.

In goal directed-movements, the deceleration phase is sometimes overlapped with submovements containing several smaller peaks.

Submovements occur when final corrections to the movement trajectory needs to be made in order to reach the goal (72). Goal-directed movements of the upper limb follow a speed-accuracy trade-off according to Fitt's law (73). Fitt's law states that the time required to move to a target is a function of the ratio between the distance to the target and the width of the target. Thus, the longer the distance to the target and smaller the target size, the more time it takes for moving towards it. The velocity profile of a goal-directed movement is nearly symmetrical when the accuracy requirements are low. The need for accuracy is increased with decreasing size of the target. When the need for accuracy is increased, the deceleration phase becomes elongated, which is more prominently seen towards the end of the movement (74). It takes longer time to grasp an object than to point and hit a target because the acceleration phase is shorter than the deceleration phase in pointing, while the opposite is true for reaching (15, 75). For fast movements, additional secondary corrections are often needed for attaining the target, due

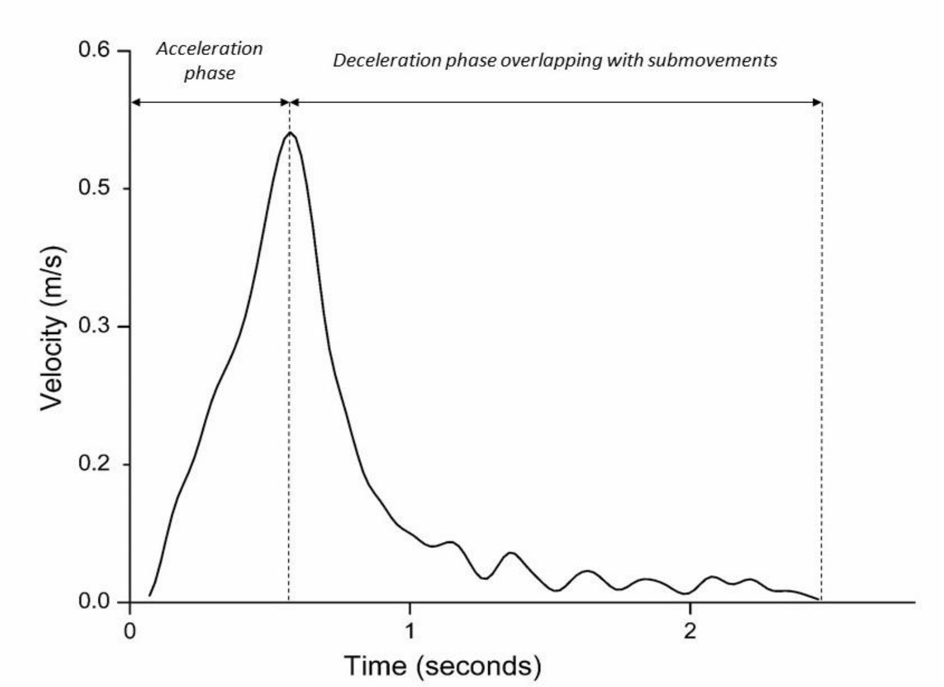

Figure 3: The velocity profile of the fast pointing task in a healthy individual.

to which a secondary corrective phase containing submovements is also seen (74).

The general shape of the velocity profile, including the relative durations of acceleration and deceleration phases remain the same when the distance to the target is increased. As a result, the peak velocity and the movement time are increased, keeping the overall shape of the velocity profile nearly intact (74). Another factor that affects the velocity profile of a goal-directed pointing task is the orientation of movement. For the same task performed in different directions, both the shape of the velocity profile and the relative durations of primary and secondary phases are affected. The shortest movement times occur when the target is in line with the subject (0 and 180 degrees), while the longest movement times occur when the target is perpendicular to the subject (90 and 270 degrees)(74). Lateral movements that involve rotation about a single joint are faster than perpendicular movements where multiple joints are involved (74).

Psychometrics of measurements

The characteristics of an outcome measure are determined by examining its psychometric properties. The three main psychometric properties are validity, reliability and responsiveness to change (76). Validity describes the degree to which a scale measures what it is supposed to measure (77). Discriminant validity involves the ability to discriminate between people of various functional levels (78). Concurrent validity involves comparing a new scale with an established measurement standard (76). Reliability describes the consistency with which results are obtained (76). Test-retest reliability is a subtype of reliability which assesses the degree to which the scores from one test administration is consistent with the next, under same testing conditions. The kinematic variables from the target-to-target pointing task used in this thesis has previously shown good test-retest reliability in healthy controls (79). Responsiveness to change is the extent to which significant changes in the subject's state are reflected in substantive changes in observed values (80).

Virtual reality (VR)

Virtual reality (VR) is a computer-generated graphical representation of the world, real or imaginary, using a three dimensional interface (81). Over the past 15 years, there has been a rapid growth in the number and type of VR applications used in rehabilitation (82). In its early days, the large size, high cost and limited accuracy were the main limitations to the use of VR in clinical practice. Between 2006-2014, low cost VR systems got introduced into the market, and off-the-shelf VR-based products that did not target healthcare came to be used by clinicians as they were user friendly and cost-efficient. High-end VR systems were also clinically tested during this period (82). From 2015-2018, VR technology became increasingly accessible, customizable and accurate. In future, VR research is likely to make significant breakthroughs, not only in the healthcare domain, but also in engineering, education and communication (83).

There are three key concepts related to virtual reality: immersion, presence and interactivity. The extent to which the user perceives that they are in a virtual environment in a VR equipment is referred to as **immersion** (84). Depending upon the range of immersion, virtual reality devices can be classified into fully immersive, semi-immersive and non-immersive. In fully immersive VR, the user feels as if they have "stepped in" to the virtual world, such as in head-mount displays. Semi-immersive VR offer limited range of immersion into virtual environment. In non-immersive VR, the virtual environment is viewed through a two-dimensional portal, such as in a video game projected on a television screen (85). VR devices also differ in terms of presence. **Presence** is the subjective experience of the individual of "feeling of being in the virtual world"(86, 87). Another related concept is **telepresence**, which is the extent to which the user feels present in the virtual environment, with the awareness of also being in the immediate physical environment (87). **Interactivity** refers to the degree to which the user can influence the form or content of the virtual reality environment (88). For VR devices, increased presence and interactivity contributes positively to immersion, and interactivity contributes positively to presence (88).

Virtual reality in rehabilitation

VR-technology has been employed in rehabilitation, particularly in motor rehabilitation (89). VR-technology has increasingly been used for stroke rehabilitation (84), and to a lesser extent, for assessment of motor function after stroke (90, 91). Virtual reality was found to be possibly beneficial in improving upper limb function and activities of daily living when used as an adjunct to usual care (84). However, high quality evidence is lacking, because the studies had a small number of participants. A recent study reported that when VR systems are specifically built for rehabilitation, it is more effective than conventional therapy after stroke (92). Despite VR systems being available for rehabilitation, their usefulness as an assessment device is not adequately explored. VR-based assessment might provide new information regarding motor function in individuals with stroke, that might not be captured using traditional clinical scales.

Some of the additional possibilities of VR-based therapy in comparison with conventional therapy for the patient are the provision to self-guide oneself, availability of naturalistic performance record and the possibility of getting real-time feedback (93). It offers therapists with an opportunity for remote data access and tele-rehabilitation (94). In addition, the VR tasks can be adapted and varied based on the level of functioning of the individual (95). Participants have reported VR tasks to be enjoyable and motivating (68, 96).

Some of the challenges in VR use in rehabilitation are related to the lack of computer skills of the therapists and patients, high initial investment, lack of infrastructure to support the equipment and communication (such as for tele-rehabilitation) and concerns about patient safety and privacy (95). There is little knowledge on if the tasks performed in VR are performed in the same way in real-world environment (97). Some tasks, such as reaching and grasping, were found to be performed using similar strategies in both real and virtual environments (98), but more research is needed to confirm if this is true for all types of tasks and devices.

Haptic technology

Haptic technology involves the use of a device to simulate rebound force (force feedback), thereby creating a perception of touching or manipulating virtual objects (99). Haptic devices can be either contact devices or non-contact devices, depending on if the device is held by the user. The common haptic devices used in VR technology are contact devices, such as gloves containing piezoelectric sensors and styli (100, 101). Pioneering research is happening in non-contact haptic technology, where air vortex ring generators or ultrasound waves can generate force feedback, but commercial devices using this technology are still under development (102, 103).

Haptic technology is perhaps more commonly used in video gaming, but it also has applications in surgical training and rehabilitation (104). Haptic devices are being tested for use in simulated operative procedures, where the doctor can practice surgical techniques on a virtual patient’s body (105). In rehabilitation, haptic technology is used for assessing and improving the function of upper and lower limbs in conditions where the sensorimotor function is impaired (106). It is also used for assessment of hemi-neglect (107). The tip of the haptic device captures the trajectory of movement in space, thereby enabling the assessment of upper limb movements in stroke. When coupled with VR, this system is able to give sensitive and accurate 3D kinematics data of movements in virtual space.

Serious games

Serious games are technology-based interventions directed towards rehabilitation rather than entertainment (108). Serious games can be used both for assessment and training, and can, in contrast to traditional assessment and rehabilitation approaches, be perceived as challenging and fun because they can offer a game-like environment, increasing levels of difficulty and possibility for customization of the game interface (108). In rehabilitation, some of the parameters that can be assessed during serious games are motor function, executive functions, visuo-motor skills, attention and memory (68, 107, 109).

Aim

The overall aim of this thesis was to validate a method for assessing the upper limb sensorimotor function following stroke using a haptic-based virtual reality technique.

The specific aims were:

Study I: To determine the discriminant validity of VR-based kinematics during target-to-target pointing task in individuals with mild to moderate arm impairment and healthy controls.

Study II: To determine the extent to which end-point kinematic variables obtained from the target-to-target pointing task are associated with upper limb impairment or activity limitation as assessed with clinical scales in individuals with stroke.

Study III: To determine when the recovery in kinematic performance of upper extremity occurs over the first year after stroke and to identify the factors that affect this recovery.

Study IV: To determine how the relationship between objective kinematic variables obtained from the target-to-target pointing task and self-reported manual ability varies during the first year in individuals after stroke.

Methods

Subjects and study design

The participants of this study were extracted from the Stroke Arm Longitudinal Study at Gothenburg University - SALGOT study. The SALGOT cohort consisted of 122 non-selected individuals with first ever stroke admitted to the stroke unit at Sahlgrenska University Hospital, Gothenburg, Sweden between 2010 and 2011 and repeatedly followed up during the first year after stroke (110).The inclusion and exclusion criteria based on the SALGOT cohort are shown in Table 1.

Table 1. Inclusion and exclusion criteria based on the SALGOT cohort (110)

Inclusion criteria	**Exclusion criteria**
stroke, determined according to WHO criteria (1) admitted within 3 days after stroke onset age >18, living in Gothenburg urban area impaired upper limb function at day 3 after stroke (FMA-UE < 66)	upper limb condition prior to stroke that limits the functional use of the arm severe multi-impairment or diminished physical condition before the stroke that would affect arm function short life expectancy due to other illness or severity of stroke injury not Swedish speaking prior to the stroke incident living outside Gothenburg

In the SALGOT cohort, each individual was assessed eight times during the first year after stroke using a battery of clinical and kinematic assessments. The assessments were carried out at 3 days, 10 days, 3, 4 and 6 weeks, 3 months, 6 months and 12 months after the stroke onset.

A total of 67 individuals with stroke from SALGOT cohort and 43 healthy controls were included in this thesis. Cross-sectional study design was used for Studies I and II while longitudinal study design was used for Studies III and IV (Table 2). In study III and IV with longitudinal data, the assessments carried out at week 3 and week 6 were excluded for analysis because these timepoints were less prioritized during data collection, and had larger amount of missing data. The flowchart of the inclusion process specified for each study is shown in Figure 4.

Healthy controls of commensurable age and gender distribution were also recruited for the study. They were included in the study if they perceived themselves to be healthy, and reported to have no neurological or musculoskeletal disorders affecting upper limb function. Exclusion criteria were: unable to follow instructions in Swedish/English and uncorrected visual acuity that influenced the test performance. Forty-three healthy controls who satisfy these criteria were recruited in 2016-17 and included in the study. Kinematic assessment was carried out only once in individuals from the control group.

Table 2. Table showing the study designs of the studies included in this thesis

Study	**Design**	**Data collection**
Study I	Discriminant validity	Cross-sectional design, both individuals with stroke and healthy controls
Study II	Concurrent validity	Cross-sectional design, individuals with stroke
Study III	Recovery after stroke	Longitudinal design, individuals with stroke, 6 timepoints
Study IV	Relationship between self-reported and objective measures	Cross sectional design at 6 timepoints

Equipment

The equipment used for the study includes a semi-immersive VR workbench, 3D shuttered glasses and a haptic device. The VR workbench has 3D display of virtual space on a mirror when looked through stereoscopic shuttered glasses. The infrared transmitter on the workbench sends signals to the shuttered glasses and synchronizes the image sequence on display, giving the participant an illusion of seeing 3D objects. A photograph of the entire equipment with a participant performing the pointing task is shown in Study I (Figure 2) and the haptic device is shown in Figure 5.

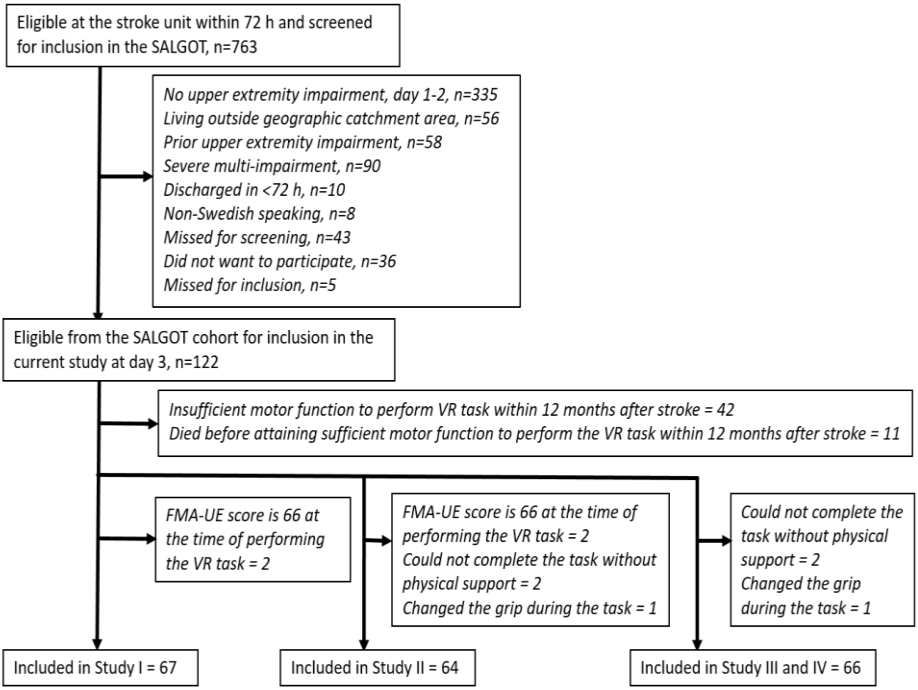

Figure 4: Flowchart of the inclusion process of the studies included in this thesis.

The PHANTOM® Omni™ haptic stylus captures kinematic data (111). It has six degrees of freedom, and its maximum exertable force is 3.3 N. The haptic stylus can be moved freely in the virtual workspace (160 × 120 × 120 mm), and it gives touch sensation and force feedback when it comes close to a virtual object, in addition to visual feedback (colour change and disappearance). Thus, the participant gets an illusion of touching and manipulating virtual objects with the stylus. The PHANTOM® Omni™ haptic stylus has previously been used for assessing the arm movements in neurological diseases and for simulating medical procedures (112, 113). An illustration showing the equipment is shown in Study II (Figure 2).

Figure 5. Phantom Omni haptic device was used in the studies included in this thesis

The target-to-target pointing task used in this study was performed using Curictus™, which is an open source software for serious games (114). After enabling the Curictus application, the haptic device was checked for calibration by confirming that there is a steady blue light in its inkwell. The participant wore 3D glasses and sat comfortably on a height-adjustable chair, such that they get the full view of the virtual space on the mirror. The participant was then asked to reach and point at a green coloured, disc shaped target using the tip of the haptic stylus. A new target appeared at another location when the previous one was pointed at and made to disappear. Each target was 3.8 cm in diameter (~ 3.0° viewing angle), with a shadow in the viewing plane. A target as is seen in the 3D space is shown in Figure 6.

The participant was instructed to perform the pointing task as fast and as accurate as possible. The participant first points at the 'Start' banner in the 3D space, after which the first target appears on the screen. No time limit was enforced, and the participant was allowed several attempts to point at the target until they become successful in making it disappear. The targets were arranged in such a way that they appear to be random for the participant, but they actually appeared in a predefined order on 9 different locations at four different depths on the screen (Figure 7). The shortest distance between two targets was 76 mm and the longest distance was 180 mm. The location of the targets in 3D space as seen from front is shown in Figure 7.

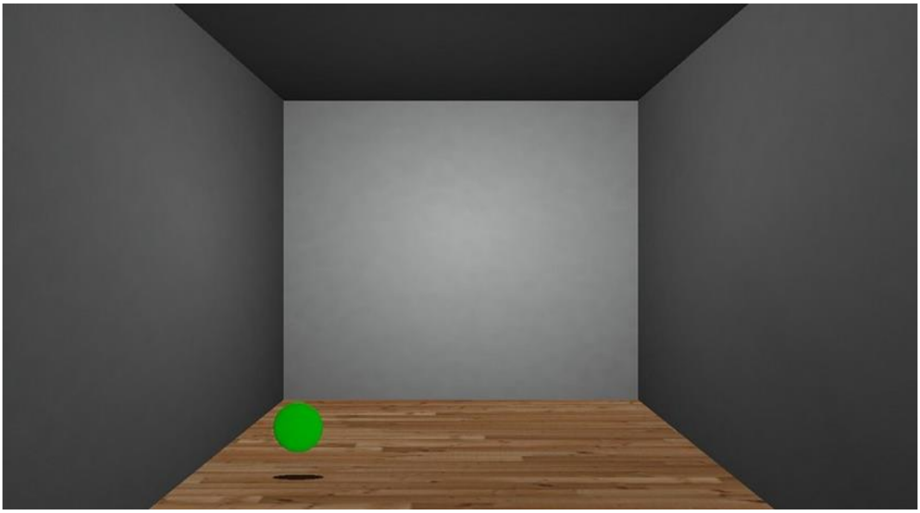

Figure 6. The target-to-target pointing task in 3D space. The participant points at the target using the haptic stylus to make it disappear.

Individuals with stroke first performed the task with their less affected arm, and then with the more affected arm. The participants were asked to hold the stylus using pen grip, but whenever pen grip was not possible due to impairment, they were allowed to use cylinder grip during the task. However, apart from three cases, all participants used the pen grip. Healthy controls performed the task in random order of arms. The task, which consisted of 32 targets, ended when the last of all targets disappeared. The participants generally performed one trial before the assessment in order to acquaint themselves with the VR setup.

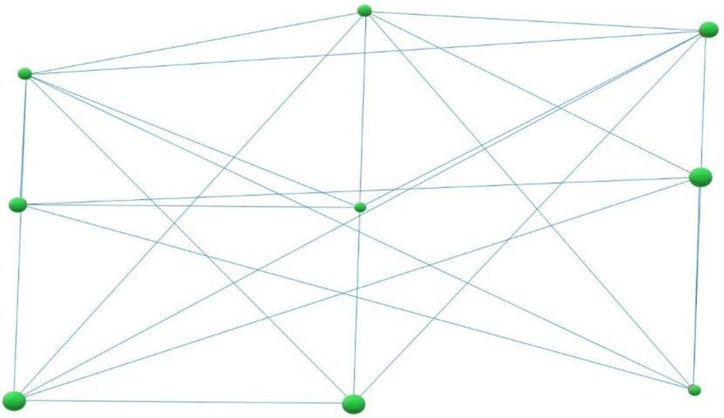

Figure 7: The locations of the targets in 3D space as observed from front along with the straight-line distances between the targets.

Kinematic measures

The time and position co-ordinates of the tip of the haptic stylus were captured using Curictus™ software. MATLAB software was used for extracting kinematic variables from the data captured by Curictus. The data was sampled at 50 Hz and filtered with a 6-Hz low pass second order Butterworth filter in both forward and backward directions. Five kinematic variables were calculated: movement time, mean velocity, peak velocity, time to peak velocity and number of velocity peaks. The algorithm used for calculation and filtering of kinematic variables has been made available on GitHub (115).

For the pointing task, the delay between hitting a target and the disappearance of the target was 0.2 second. The delay between disappearance of one target and appearance of a new target was 0.1 second. All kinematic variables were reported inclusive of these delays.

The entity between two adjacent targets was called movement segment. For the 32 targets included in this study, there were 31 movement segments. The first segment between the 'Start' banner and the first target was excluded for analysis. All kinematic variables were calculated as means of all 31 movement segments for the entire task. Table 3 shows the list of kinematic variables included in this thesis, with descriptions.

Table 3. Kinematic variables included in this thesis with descriptions

Kinematic variable	**Description**
Movement time	Mean of the times taken to complete each movement segment
Mean velocity	Mean of the velocities of each movement segment
Peak velocity	Mean of the maximum absolute velocity of each movement segment
Time to peak velocity	Mean of the time taken to reach the peak velocity for each segment, expressed in percentage of movement time
Number of velocity peaks	Mean of the number of velocity peaks of each movement segment. Velocity peak was defined as the difference between a local minimum and the next maximum in the velocity profile, whenever the difference between them exceeded a cut-off of 20 mm/s. In addition, the time between two subsequent peaks had to be at least 150 ms.

Other kinematic variables that were considered for the kinematic analysis included hand-path ratio and acceleration. Hand-path ratio, defined as the ratio between the length of the actual movement trajectory and a straight line representing the shortest distance to the target, is often used to quantify the movement performance in stroke (60, 79). The trajectory of arm movement during natural functional activities are commonly curved rather than following a straight line. Similarly, acceleration, the third derivative of distance, has higher noise, which makes the interpretation of this metric less certain. Our aim was to include only the most effective and potential measurements, so the number of kinematic variables in this thesis was limited to five (60, 116).

In Studies I and II, all five kinematic variables were considered for analysis. In studies III and IV, all variables except time to peak velocity was included in the analysis. Time to peak velocity showed neither discriminant validity with healthy controls nor concurrent validity with clinical scales. Therefore, it was removed from analyses in the later studies in order to limit the number of statistical analyses performed and to present only the relevant results.

Clinical measures

The demographic data including age, sex, side of stroke paresis, dominant hand, type of stroke etc. of all participants were recorded. In the SALGOT study, a battery of clinical assessments was performed. However, in this section, only the assessments used in this thesis are described further.

Fugl-Meyer Assessment of Upper Extremity (FMA-UE) was performed to determine the sensorimotor function of upper limb (117, 118). FMA-UE is an ordinal scale that is widely used to evaluate post-stroke upper limb function (54, 117). It has 3 points for each item. The motor domains of FMA-UE have been divided into upper extremity, wrist, hand and co-ordination. Full arm function is indicated by a maximum score of 66 in the FMA-UE scale. The three non-motor domains of FMA-UE are sensation, passive joint motion and joint pain. FMA-UE scale has excellent reliability (119-122) and high degree of concurrent validity of its motor domain with Action Research Arm Test (ARAT) (123). For Study I, participants were divided into two groups based on their FMA-UE score as moderate stroke impairment (FMA-UE score: 32-57 points) and mild stroke impairment (FMA-UE score: 58-65 points) (124-126).

Action Research Arm Test (ARAT) was performed for assessing the activity capacity of the upper limb (127). ARAT is an ordinal scale that consists of 19 items, which are divided into four hierarchical subsets (grasp, grip, pinch, gross movement). Higher scores show that the individual has higher manual activity capacity. The maximum possible score is 57 points. ARAT has excellent reliability (127-129) and its concurrent validity against FMA-UE scale (123), arm subscore of Motoricity Index and upper extremity part of Modified Motor Assessment Chart have been established (129).

ABILHAND questionnaire was used to measure the self-reported manual ability (130). ABILHAND evaluates the individual's perceived difficulty in performing daily bimanual tasks. It contains 23 items, where each item is classified as impossible (0 point), difficult (1 point) or easy (2 points). A question mark symbol is recorded when an activity presented in an item was not attempted. ABILHAND uses Rash analysis methodology to convert raw ordinal data into a continuous, unidimensional scale with scores presented as logits (131). Higher ABILHAND logits imply better self-reported manual ability. ABILHAND logits were calculated by entering the raw test scores into a Rasch analysis online module hosted at www.rehab-scales.org, which gave an evaluation report containing ABILHAND logit score, standard error and missing responses for each individual.

National Institute of Health Stroke Scale (NIHSS), Modified Ashworth Scale (MAS) scoring and Barrow Neurological Institute (BNI) pre-screening were included in the background data. NIHSS scoring was performed to determine the stroke severity at the time of hospital admission (132). Modified Ashworth Scale (MAS) was performed to assess muscle spasticity of the muscle groups of elbow flexors and extensors as well as wrist flexors and extensors (133). BNI was performed to pre-screen the level of alertness, basal communication and co-operation (134).

Data analyses

Statistical methods

The statistical data analyses were done using MATLAB R2018b and IBM SPSS (Statistical Package for Social Sciences) version 24. A significance level of 0.05 was used in all statistical analyses and Bonferroni correction method was applied whenever multiple comparisons were performed. Descriptive statistical methods were used for describing groups of subjects in terms of demographic characteristics, clinical features and kinematic movement performance measures. Analytical statistical methods were used for determining the difference and relationship between groups, change over time and agreement (Table 4).

Table 4. Statistical methods used in this thesis

Analytical statistical methods	**Studies**			
	I	II	III	IV
Analyses of difference between groups				
Wilcoxon's signed rank test	×		×	
Kruskal-Wallis one-way analysis of variance	×			
Mann-Whitney U test	×		×	
Effect size (Point biserial correlation)	×		×	
Analyses of relationships				
Spearman rank-order correlation		×		×
Univariate and multiple linear regression		×		
Analyses of change over time				
Linear mixed model			×	
Effect size (Point biserial correlation)			×	
Analyses of agreement				
Sensitivity/specificity	×			

Discriminant validity (study I)

In Study I, non-parametric statistics were used as a majority of variables were non-normally distributed. Mann-Whitney U test was first used to determine if there were significant differences between the arm function in individuals with stroke and healthy controls. Kruskal-Wallis one-way analysis of variance was then used to determine the differences between individuals with mild stroke impairment, moderate stroke impairment and healthy controls. If Kruskal-Wallis test showed significant difference between groups, Mann-Whitney U test with Bonferroni correction was used for post-hoc testing. Point biserial correlation (r_{pb}) was used to calculate effect sizes, where 0.1, 0.3 and 0.5 indicate small, medium and large effect sizes respectively (135). Sensitivity and specificity were calculated for those variables that showed significant differences between individuals with stroke and healthy controls. One standard deviation (SD) of the corresponding kinematic variable for healthy controls was determined as the cut-off for calculating sensitivity and specificity.

Concurrent validity (Study II)

Multiple regression with forward addition was used to determine the amount of variance in FMA-UE and ARAT clinical scales that can be explained by five kinematic variables. Along with the five kinematic variables, age, side of paretic arm, time since stroke and severity of stroke impairment at onset (NIHSS score) were included as independent variables. Pearson's correlation coefficient was calculated between pairs of all independent variables, and those with correlation coefficients greater than 0.7 were not included in the same model (136).

Univariate regression was first done, where variables with p-value less than 0.2 were added to multiple regression model building, one at a time, starting with the variable that has the lowest p-value. However, in the final models, only those variables with $p<0.05$ were retained. When the final model was generated, each of the confounding variables were added and they were retained if they increased the R^2 value by at least 5% ($p<0.05$). The assumptions for multiple regression were verified for all final regression models.

Analysis of change over time (Study III)

In Study III, natural log transformation (ln) was performed on all dependent variables so that they were approximately normally distributed. The significance levels for statistical analyses were set to $p<0.05$. In order to assess the longitudinal changes over time, linear mixed model analysis was performed. An initial model with fixed effect of time, random effect of time and intercepts was created. Fixed effects of cofactors, namely, stroke severity, age, type of stroke, side of stroke paresis, sex and presence of diabetes were added one at a time into the model. The interaction effect of significant cofactors with time was tested. In order to determine the significance of the new model with the added variable against the base model, log likelihood ratio test was used. The residual plots of final models were checked for linearity, constant variance and normal distribution.

Whenever fixed effect of time was found, Wilcoxon's signed rank test was used to find the time points between which significant differences exist. To interpret the strength of the difference between groups, effect size estimate was used, and Cohen's guidelines were used for interpreting the effect sizes (135). In order to determine if significant differences exist between individuals with stroke at all timepoints and healthy controls, Mann-Whitney U test was performed. Bonferroni correction was applied to the p-values for both Wilcoxon's signed rank test and Mann Whitney U test and the level of significance was set to 0.008.

Analysis of relationships (Study IV)

In Study IV, Spearman's correlation coefficient was used to measure the correlation between ABILHAND logits and four kinematic variables. The strength of correlation coefficients was interpreted as 0.00-0.25 (very low), 0.26-0.49 (low), 0.50-0.69 (moderate), 0.70-0.89 (high) and 0.90-1.00 (very high) (136). As 24 pairs of variables were compared, Bonferroni correction was applied, and the p-value required for significance was adjusted to <0.002.

Ethical considerations

All four studies included in this thesis were approved by the Regional Ethical Review Board in Gothenburg, Sweden. The approval protocol numbers for studies I and III were, 549-03 for recruitment of healthy controls and 225-08 for individuals with stroke. For studies II and IV, the protocol number was 225-08. All participants gave informed written consent prior to their participation in the studies. Participants were given full information about the assessment procedure and they were allowed to discontinue their participation without having to provide an explanation. They were allowed to take rest between assessments. If any issues arose during the assessments, the participants could discuss them freely with the test leader. The participants were also provided information regarding data handling and confidentiality.

No specific risks were identified prior to, during or after the assessment. The SALGOT clinical trial was registered at https://ClinicalTrials.gov (Identifier: NCT01115348).

Results

The stroke group consisted of 67 individuals extracted from the SALGOT cohort. The background data of stroke group are shown in Table 5. The kinematic data of the non-dominant arm of the healthy group (n=43) served as a reference to compare with the stroke group. The choice of using the kinematic variables from the non-dominant arm instead of the dominant arm was to put those with paresis in the non-dominant arm in the stroke group at less of a comparative disadvantage (23). The mean age of the healthy group was 64.9 (SD: 14.0) years and females constituted 46.5% of the healthy group.

Table 5. Demographic characteristics of the stroke group

Demographic data, clinical characteristics and assessments at admission (n=67)	**Mean ± SD, n (%) or median (Q1-Q3)**
Age	65.7 ± 13.6
Female	27 (41%)
Ischemic/haemorrhagic stroke (%)	82/19
Right hand dominant	64 (95%)
Right hemiparesis	29 (44%)
NIHSS total score	6.2±5.1
Diabetic status	7 (10%)
FMA-UE score (max. score = 66)	58 (54-62)
Score <9 in BNI pre-screening	5 (7%)
Decreased sensation (≤11 points, FMA)	6 (10%)
Pain during passive movements (≤23 points, FMA)	5 (10%)
Spasticity of the elbow or wrist joint (≥ 1 point MAS)	1 (1%)

Discriminant validity (Study I)

A majority of the kinematic variables were found to be discriminative between individuals with mild stroke (FMA-UE score 32-57) moderate stroke (FMA-UE score 58-65), as well as healthy controls. In differentiating between stroke group and healthy control group, the kinematic variables of movement time, mean velocity and number of velocity peaks showed high effect size (>0.5).

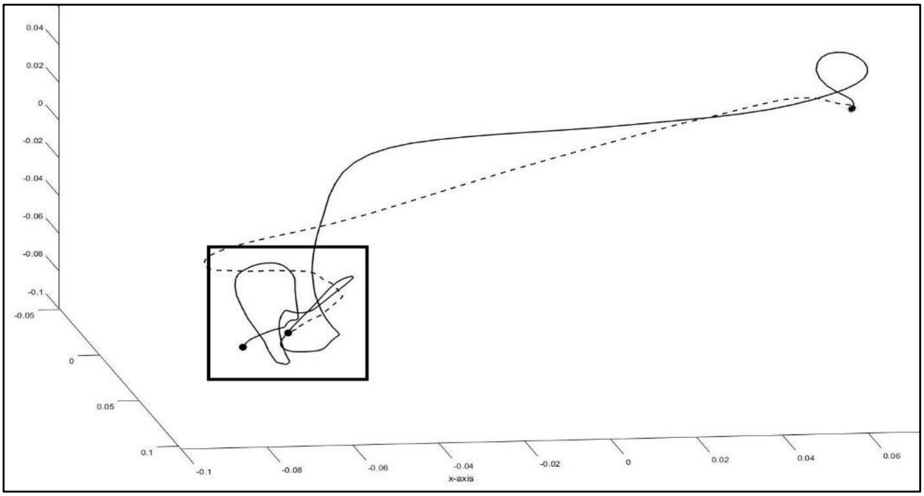

Figure 8. Trajectory of one movement segment in 3D space shown for one individual with stroke impairment (solid line) and one healthy control (dashed line). The box shows spider-webbing towards the end of the trajectory.

Movement time, mean velocity and peak velocity showed differences between individuals with mild and moderate stroke impairment. Similarly, movement time, mean velocity and number of velocity peaks showed differences between individuals with mild stroke impairment and healthy controls. The trajectories of some individuals with stroke showed clustering (spider-web) pattern towards the end of the movement segment (Figure 8). A full numeric description of the results can be found in Study I, Table 2. The kinematic parameters of the more affected and less affected arms of individuals with stroke and healthy controls are shown in Table 6. The sensitivity and specificity of the kinematic variables for discriminating between individuals with stroke and healthy controls are tabulated in Table 7. The effect sizes of differences between individuals with mild and moderate stroke, as well as healthy controls are shown in Figure 9.

Movement time ($p=0.001$, $r_{pb} = 0.48$) and number of velocity peaks ($p<0.001$, $r_{pb} = 0.53$) also showed significant differences between the less-affected arm of individuals with stroke and the non-dominant arm of healthy controls (Table 6).

Table 6: Kinematic parameters of the more affected and less affected arms of individuals with stroke. Kinematic variables of the less-affected arm showing significant differences with healthy controls are marked in asterisks.

Kinematic parameter (mean±SD)	**Individuals with stroke**		**Healthy controls**
	More-affected arm	**Less-affected arm**	**Non-dominant arm**
Movement time (s)	2.80 ± 1.97	1.90 ± 1.07*	1.31 ± 0.25
Mean velocity (mm/s)	144.8 ± 59.74	178.20 ± 62.3	209.2 ± 48.86
Peak velocity (mm/s)	374.8 ± 134.6	480.10 ± 137.1	440.7 ± 91.81
Time to peak velocity (%)	31.34 ± 9.87	34.55 ± 13.35	33.29 ± 10.51
Number of velocity peaks	4.76 ± 2.65	3.18 ± 1.45*	2.80 ± 0.53

Table 7: Sensitivity and specificity of the kinematic variables of the pointing task in Study I

Kinematic variable	Cut-off value	Sensitivity (%)	Specificity (%)
Movement time (s)	1.56	82.1	86.1
Mean velocity (mm/s)	160.34	70.2	83.7
Peak velocity (mm/s)	348.89	46.3	93.0
Number of velocity peaks	3.33	64.2	83.7

Concurrent validity (Study II)

There were significant correlations with FMA-UE and movement time (0.40), mean velocity (0.37), number of velocity peaks (− 0.35) and peak velocity (0.28). ARAT showed significant correlation with movement time (− 0.40), number of velocity peaks (0.36) and mean velocity (0.28). Multiple regression of kinematic variables showed that mean velocity and number of velocity peaks explained 11 and 9 percent of the FMA-UE score uniquely and 16% of the score when taken together. Movement time explained 13% and number of velocity peaks explained 10% of ARAT score. The confounding variables of age, side of paretic arm, time since stroke and severity of stroke impairment (NIHSS score) at stroke onset did not influence the final multiple regression models. The results of univariate and multivariate regression of kinematic variables against clinical scales can be found in Tables 2 and 3 of Study II respectively.

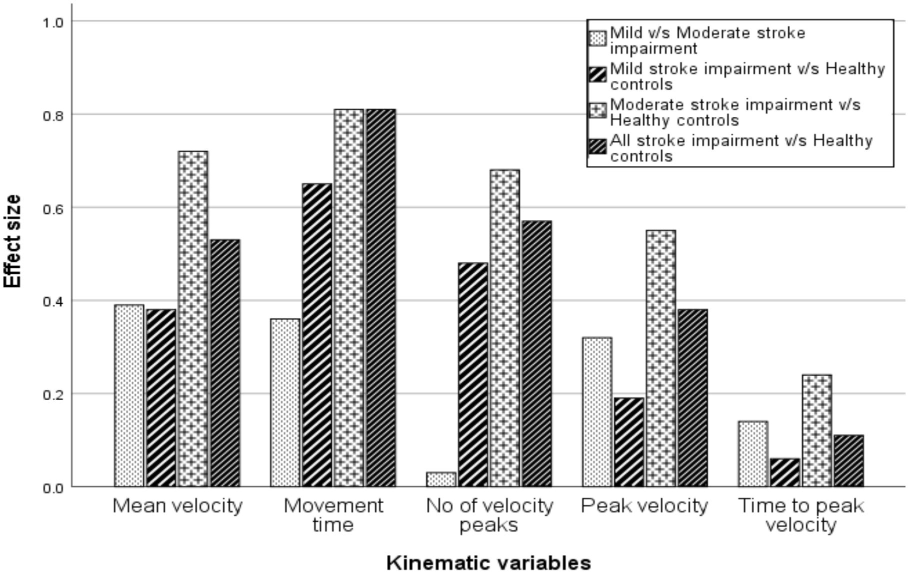

Figure 9. Figure showing effect size of the difference between various levels of stroke and healthy controls

Longitudinal change (Study III)

A significant fixed effect of time was found for kinematic models of movement time, mean velocity and number of velocity peaks between day 3 and month 12 after stroke. In these three models, younger age, less severe stroke and ischemic stroke compared to hemorrhagic stroke influenced the effect of time positively. Additional factors that positively influenced the model for mean velocity were female sex, being non-diabetic and having right-sided paresis. No random effect of time or interaction between effect of time and cofactors was found. A table containing the results of the mixed model analysis can be found on Table 2 of Study III.

Most of the improvement in kinematic arm function occurred during the acute and subacute stages after stroke, but some improvement was found at the late subacute stage after stroke. A summary of comparison of kinematic variables between adjacent timepoints can be found in Table 8.

When kinematic variables at all timepoints were compared with that of healthy controls, movement time and number of velocity peaks were found to be different from healthy controls at all timepoints except at 6 months after stroke. Mean velocity was different from healthy controls at 3 and 10 days after stroke, and peak velocity at 3 days after stroke.

Relationship with self-reported assessment (Study IV)

The correlation between self-reported and objective assessments was very low or low at the subacute stage of stroke, but became moderate at the chronic stage. Specifically, the correlation of ABILHAND logits with movement time and mean velocity was low to very low until month 6 after stroke, but became moderate to high at month 12. For peak velocity, the correlation coefficient remained very low to low throughout the course of one year after stroke. Number of velocity peaks showed very low to low correlation until month 3 after stroke and moderate correlation from 6 to 12 months after stroke. The full numerical description of correlation coefficients between ABILHAND logits and kinematic variables from day 3 to month 12 after stroke can be found in Table 2 of Study IV.

Non-included and missing individuals

The SALGOT cohort consists of an unselected group of individuals admitted at the stroke unit in Sahlgrenska University Hospital, the largest in Gothenburg, Sweden. All individuals with stroke in the Gothenburg urban area are admitted to one of the three stroke units at Sahlgrenska University Hospital depending on where places are available.

The largest stroke unit, from which the participants included in this thesis were enrolled, includes all patients who were potential candidates for reperfusion. At the time of this study, only about 10% of all stroke patients admitted to Sahlgrenska received reperfusion treatment (most commonly, thrombolysis). Hence, it can be assumed that the individuals admitted in the largest stroke unit at Sahlgrenska are representative for the stroke population in large and that the selection bias was small. Studies III and IV were longitudinal studies, and the number of participants varied at different time points. This happened either due to missing data or due to insufficient motor function for performing the pointing task. The commonest reasons for missing data were difficulties in attending the assessment sessions, presence of other medical problems, being affected by a new stroke and technical problems related to the equipment. The details regarding missing data are given in the supplementary file of Study III.

Table 8. Effect size and p-value of the comparison between adjacent time points from day 3 to month 12 after stroke. Bolded digits indicate significant differences.

Effect size and p value	**Day 3 and day 10 (N =27)**	**Day 10 and Week 4 (N=38)**	**Week 4 and Month 3 (N=42)**	**Month 3 and month 6 (N=45)**	**Month 6 and Month 12 (N=42)**
Movement time	0.67 (0.001)	0.75 (<0.0001)	0.34 (0.03)	0.51 (0.001)	0.07 (0.66)
Mean velocity	0.53 (0.006)	0.56 (0.001)	0.43 (0.006)	0.31 (0.04)	0.22 (0.16)
No. of velocity peaks	0.41 (0.03)	0.65 (<0.0001)	0.13 (0.40)	0.45 (0.003)	0.08 (0.60)

Discussion

Main findings

This thesis provides a detailed description about the kinematic movement analysis of the target-to-target pointing task in virtual reality. Movement time, mean velocity, peak velocity and number of velocity peaks were discriminative for arm function of groups with moderate to mild stroke impairment, as well as healthy controls. Movement time and number of velocity peaks were also discriminative for the more-affected and less affected arm in individuals with stroke. Mean velocity and number of velocity peaks explained 11% and 9% of the FMA-UE score respectively, while movement time and number of velocity peaks explained 13 % and 10 % of ARAT score respectively. Taken together, movement time and number of velocity peaks explained 16% of FMA-UE score and 10% of ARAT score. Age, side of the paretic arm, time since stroke and stroke severity did not affect the association of kinematic variables with FMA-UE and ARAT.

The kinematic variables of movement time, mean velocity and number of velocity peaks showed improvement over time and were affected positively by younger age, less severe stroke and ischemic compared to hemorrhagic stroke during the course of one year after stroke. The recovery of upper limb after stroke measured using kinematic variables occurred maximally before 3 months, but continued between 3 and 6 months after stroke. Except for the measurement at 6 months, movement time and number of velocity peaks differed significantly from that of healthy controls at all timepoints within one year after stroke. The correlation of kinematic variables with self-reported outcomes varied during the first year after stroke. The correlations were low or very low early after stroke, which became moderate to high after 6 months for movement time and number of velocity peaks, but remained low to moderate for mean velocity and low for peak velocity.

The kinematic variables of movement time and number of velocity peaks were found in overall to be the most useful variables for the assessment of arm impairment using pointing task in virtual reality.

These measures showed discriminant validity between various levels of impairment in individuals with stroke and healthy controls, concurrent validity with FMA-UE and ARAT scales and longitudinal validity from acute to chronic stage of stroke.

Methodological considerations

Kinematic characteristics of upper limb tasks have been analyzed in several studies performed in healthy controls. It has been well established that experimental constraints, such as, task goal, target size and location affect the movement trajectory (73, 74, 137, 138). The presence of a target makes the movement smoother, faster, more forceful and more pre-planned in individuals with stroke (137). For example, as the size of the target increases, the deceleration phase of the bell-shaped velocity profile becomes longer for the pointing task (74). With increasing distance, the entire velocity profile is elongated, without differentially influencing the phases of the velocity profile (74). Interestingly, movement time was longer while pointing to a slippery target (fur) compared to a rough target (sandpaper) presented on a monitor (139). Here, the increase in movement time was due to a relatively longer deceleration phase. Horizontal movements that involve movement at a single joint are faster than vertical movements involving more than one joint (74). Whether the task includes grasping or not also influences the reaching kinematics (15). In grasping, the deceleration phase of the velocity profile was longer compared to that of pointing at a target (75).

The peak velocity is higher and movement time is lower for competitive tasks compared to co-operative tasks as well as for social tasks compared to solo tasks (140). Similarly, if the task was first demonstrated by an actor, individuals tend to imitate the velocity of the actor’s movements, perhaps due to direct visuo-motor mapping of the task. The individuals imitated the actor’s velocity when the task was goal directed, but not when the task was non-goal directed (141). Similar imitation of velocity was found also when the task was demonstrated by an avatar in virtual reality (142). However, the individuals demonstrated no difference in velocity between movements demonstrated by socially engaged avatars (who smiled at the participant) and socially disengaged avatars (142). Thus, it is probable that virtual reality has limitations in terms of providing social engagement. In addition, there are differences in performing the pointing task when viewed using head mounted display or large screen projection system, indicating that the viewing medium also interferes with the subsequent arm movement (143). Thus, it is evident that methodological differences across studies result in difference in outcomes. As a result, it becomes difficult to compare the results of kinematic studies. Standardization of measurements in stroke kinematics is the best solution for enabling the comparison and meta-analyses of the growing body of kinematic studies (53, 65).

In order to understand the specific difficulties that the individual faces during daily life, daily life tasks such as the pointing task used in this thesis should be subjected to research. The pointing task used in this thesis analyses a commonly performed, purposeful task from real life, giving it good ecological validity. Movements in virtual environment are considered sufficiently similar to the real world, with the exception that movements were slower for healthy controls and less accurate for individuals with stroke in VR compared to real-life (144).

The haptic device used in the present study has also been used in studies related to Parkinson’s disease (145), Friedreich’s ataxia (145), multiple sclerosis (113, 145), muscular dystrophy (145) and traumatic brain injury (146). Tasks involving manipulating an object using haptic device were able to differentiate between individuals with multiple sclerosis and healthy controls (113). The haptic device was used to graphically describe the course of arm movement within a maze in individuals with Friedreich’s ataxia and other neurodegenerative diseases (145). People with chronic traumatic brain injury reported being engaged while performing haptic-enabled virtual reality tasks (146).

Data collection and handling

In the equipment used for capturing kinematic data in this thesis, a simple pointing task was used, during which end-point kinematics were measured. Due to task and equipment constraints, some aspects of movement performance, such as joint angles and trunk displacement could not be ascertained using the equipment used in this thesis. On the other hand, this equipment allows for capturing movements from six degrees of freedom, which is an advantage compared to certain robotic exoskeletons that provide movements only in specific planes and within limited range of motion.

For use in clinical settings, the equipment should be easy to set up and handle, have an intuitive interface, provide quick assessment, show easily interpretable results and have low maintenance costs. It is an added advantage if the apparatus is useful for other purposes, such as for providing rehabilitation. The equipment used in this thesis can be set up and handled in a similar way as any plug-and-play device. The interface of the software is intuitive and simple, and doesn't require any specific computer skills. In clinical applications of the VR-device, the participant can get feedback regarding their movement time and velocity metrics as soon as the task is completed. Detailed kinematic data could be made available for the researcher for offline analysis. The equipment used in this thesis was available in some wards for stroke rehabilitation (Sahlgrenska University Hospital in Sweden and Sunnås Hospital in Norway) at the time of this study.

Given that technology has progressed very much over the years, it is imperative to consider the use of upgraded hardware and software systems instead of the equipment used in this thesis. The stationary haptic device could be replaced with a bluetooth-enabled free stylus, the targets could be visualized with more resolution using high-end software and the display system could be mounted within a head-mounted display, instead of mirroring it from the monitor display. The pointing task could be made available at various levels of difficulty, including targets of different sizes, distractor targets that fetch negative points and wider working space. The same task could be modified to also assess hemi-neglect, a common problem encountered in individuals after stroke (107). However, the general characteristics of the pointing task and the kinematic variables identified in this thesis are valid regardless of the recentness of the equipment. With virtual reality technology progressing at a fast pace, features that seem difficult to incorporate, or even unfeasible today might become everyday reality in future.

The software for the VR-pointing task used in this thesis was developed by a research-based company in collaboration with the University of Gothenburg. When the company closed down, the continued updating and maintenance of the software were stalled, and the software could not be run on computers with newer versions of operating systems. This is, unfortunately, a widespread problem in rehabilitation. A continuous software support and updates of the device hardware are needed for prolonged use of the equipment both in research and in clinical praxes.

For analyzing the kinematic data used in this thesis, the author developed her own algorithm using MATLAB. Presently, most of the software used for kinematic analysis lack user-friendly interface. As a result, researchers need to develop their own custom-made algorithms for data analyses. The tools for gathering kinematic data have different specifications and data structures, which also makes it difficult to create a software that analyses all types of kinematic data. For kinematic analysis to become more widespread in clinical settings, it is important to have software with simple interface where clinicians can perform the assessment procedure using a wide variety of data structures and interpret the results with ease.

Validation of kinematic variables

A large part of this thesis deals with validating end-point kinematic analysis for assessment of upper limb function after stroke. Kinematic analysis can offer a platter of unlimited number of variables, but not all of them are meaningful for assessment of arm function. For this thesis, kinematic variables that demonstrate face validity were first chosen. This choice was influenced by graphical representation of kinematic data, which was also compared with the kinematic data from other studies related to upper limb kinematics in stroke.

Choosing the most appropriate kinematic variables requires a good understanding of the mechanism of motor control, nature of the task, nature of arm impairment of the participants and knowledge of available computational methods. An ideal kinematic variable should be easy to calculate, easily interpretable, comparable to the variables from other studies and possibly start its measurement from absolute zero. The kinematic variables used in this study are easy to interpret, and common terms such as duration, speed, smoothness could be used to describe some of them. These variables don't require very complex programming and the methods used were comparable to similar studies, although the chosen cut-offs were specific for the equipment and the task. The pointing task requires the ability to hold and move a haptic stylus in the arm's workspace, which makes the test suitable only for those with mild to moderate arm impairment and therefore, those with severe arm impairment could not be analyzed using this task.

Discriminant validity (Study I)

Several studies in stroke rehabilitation have investigated the discriminant validity of kinematic variables between individuals with stroke and healthy controls (116, 147-149) as well as between the less affected and more affected limbs of individuals with stroke (90). These studies used diverse tasks, such as moving a centrally located target to peripheral targets (90), performing planar pointing movements with or without exoskeleton (147-149) and drinking water from a glass (116). Regardless of the diversity in tasks used, most results from these studies were similar to each other and to Study I. In general, movement time was longer (90, 147), mean and peak velocities were lower (90, 116, 148) and number of velocity peaks was fewer (90, 116, 148, 149) in individuals with stroke compared to that of healthy controls. In Study I, time to peak velocity did not show differences between individuals with stroke and healthy controls, in contrast to a previous study using self-paced reaching task (116). Thus, it is possible that the speed of the task or other task characteristics affect the discriminant validity of kinematic variables, at least in some cases.

Relatively few studies have reported the differences in kinematic performance between individuals with mild and moderate stroke impairment of the upper limb (116, 150). In Study I, movement time and mean velocity were discriminatory for both mild and moderate stroke impairment as well as healthy controls. Peak velocity could discriminate between mild and moderate stroke impairment, but not between mild stroke and healthy controls. Contrary to this, smoothness could discriminate between mild stroke impairment and healthy controls, but not between mild and moderate stroke impairment. Hence, it is possible that peak velocity is an appropriate variable when motor function is poor, and smoothness is useful when higher levels of function is reached. In a related study, when the participants of the same cohort performed "reaching and drinking" task, movement time, peak velocity, time to peak velocity, smoothness and other three kinematic variables discriminated between mild and moderate stroke impairment and healthy controls (116). Thus, it is possible that the reaching-and-drinking task is more sensitive than the pointing task in terms of discriminating between various levels of functional impairment after stroke and healthy controls. More studies are needed for establishing which kinematic variables and tasks are robust for discriminating between various functional levels after stroke.

The data from this thesis showed that there were significant differences between the less affected arm of individuals with stroke and healthy controls in terms of movement time and smoothness. A similar study involving the drinking task showed that the movements of the less-affected arm in individuals with stroke are slower and less smooth compared to healthy controls early after stroke (23). Another study examining reach-to-grasp movements has also concluded that the smoothness of movement of the less-affected arm is lower than that of healthy controls (91). All these point to the fact that kinematic analysis may also be suitable for assessing the arm function of the less-affected arm in individuals with stroke.

Concurrent validity (Study II)

Study II shows that kinematic variables could only explain a part of the variance in clinical scores of upper limb function and activity capacity. Slightly higher variance of FMA-UE than ARAT is explained by kinematic variables, showing that kinematic variables of the pointing task are probably more strongly correlated with 'Impairment' than 'Activities' of the ICF model. Further research is needed to confirm this hypothesis.

Motion capture studies that examine the concurrent validity of kinematic variables report that 13 to 57 percent of variance of clinical scales can be explained using kinematic variables (151-153). On the other hand, robotic studies that examine the correlation between kinematic variables and scores from clinical scales show that the correlation coefficients for mean velocity and number of velocity peaks varied between 0.01-0.7 and 0.02-0.5 respectively (154). The large variability in terms of association between kinematic variables and clinical scales scores in these studies is probably due to the difference in the type of task used, pace of arm movement, type of clinical scale used as the outcome measure and task constraints.

The low variance explained by Study II could be because of several reasons. The traditional clinical scales do not have as much sensitivity for detecting smaller differences in movement quality as kinematic variables (63, 155). This difference in sensitivity might have contributed to the low explained variance between them. The kinematic variables from quick pointing task might not show as much explained variance with movements and reach-to-grasp tasks performed within FMA-UE and ARAT since the speed at which the task is performed during these clinical assessments is not given high importance. The relatively small workspace of the pointing task compared to the range of movement required for performing FMA-UE and ARAT would also be a reason for the low variance.

Change over time (Study III)

The factors found to influence the recovery of kinematic variables positively, such as lower stroke severity, lower age and ischemic type of stroke compared to hemorrhagic type were also known to affect clinical recovery (44, 46, 49). Mean velocity was additionally higher for female sex, those with right sided stroke paresis and non-diabetic individuals. The right hand being the dominant one (156) and impairments due to diabetes might be the reasons for this phenomenon. Except for peak velocity, all kinematic variables showed a non-linear recovery pattern, similar to that of the recovery pattern of clinical scale scores (20).

In study III, improvement in movement time and smoothness were found beyond 3 months after stroke, while most clinical studies have shown recovery only up to 3 months (20, 44). It is likely that kinematic variables are more sensitive towards detecting recovery during the subacute stage of stroke. Study III showed that movement time and smoothness reach at par with healthy controls at the 6th month, but decline again by the 12th month after stroke. The reason for this decline is probably because rehabilitation provided by the healthcare system might have ended after 6 months' post stroke. Individuals with stroke are likely to fall back to lower level of arm function if continuous training is not available.

Relationship between self-reported and objective assessments (Study IV)

The relationships between self-reported manual ability and objective kinematic measures were the weakest early after stroke. The reason for this phenomenon could be that individuals in the acute stage of stroke might not have had enough time to fully perceive how their arm impairment due to stroke could affect their ability to perform daily bimanual tasks. At later time points, the correlations, in general, were stronger compared to earlier time points. This could indicate that the self-perceived manual ability gets closer to objectively assessed manual ability with time. It was movement time and number of velocity peaks that showed the most increase with time. Thus, it is likely that slowness (longer movement time) and clumsiness (less smooth movements) are more easily perceived by individuals in daily life than other aspects of kinematic performance.

A past study showed that the correlation between kinematic variables from the drinking task and ABILHAND logits is low at the subacute stage of stroke (151). In the chronic stage of stroke, the correlation between self-perceived amount of arm use and FMA-UE score was found to be moderate to high, and individuals needed high functional ability to be able to utilize their affected arm in daily activities (26, 27). Among persons with full or nearly full arm function scores, the proportion of those who self-report residual disability is as high as 20-40% (28, 29). All these findings are in line with the findings from Study IV.

While setting individual goals for stroke rehabilitation, one of the main barriers is the gap between clinicians' and patients' perspective (157). While clinicians act based on the objective assessments, patients are likely to act based on their perceived function. From Study IV and similar studies, it is clear that there exists a discrepancy between self-reported manual ability and objectively assessed arm function, particularly during the early stages of stroke. Therefore, it is more effective to use a combination of self-reported and objective assessments in order to have a better understanding of the individual's perspective after stroke.

Strengths and limitations

The main strength of the studies included in the current thesis is the relatively large and unselected study sample where participants were assessed from as early as day 3 until month 12 after stroke. Such a large unselected group covering all stages of stroke has seldom been reported in previous robotic kinematic studies that examine discriminant, concurrent and longitudinal validity in people with stroke. Many robotic systems are often restricted to kinematics captured in 2D space, while the haptic device used in this study, similar to camera-based or sensor-based systems, allow for free movements. The participants reported that the pointing task was entertaining and motivating, which shows that it was well-accepted (68). The equipment used for this study is less expensive compared to other assessment methods such as optoelectronic cameras and exoskeletons, making it a good candidate for use in community settings and home rehabilitation.

The studies mentioned in this thesis are not without limitations. The pointing task used in this study can be performed only if the participant has a certain level of arm function. Therefore, the results from this study can be generalized only to individuals with moderate to mild stroke impairment. The haptic device allows for capturing only the end-point kinematic data, so it is not possible to capture the movements at joint levels and trunk. Hence, it is not possible to determine whether the movement was accomplished with normal or altered joint configurations, using this method.

Clinical implications

The choice of the assessment method plays an important role in how rehabilitation interventions are evaluated. It is important to choose the right assessment method for the context to be able to produce results that are useful and appropriate for the given research question. In clinical settings, specific upper limb assessment is not always prioritized and technology-based measures are rarely used. The reason for this is can be the limitation in time and resources, but also the knowledge and access to the technology. VR-based tasks are intuitive, motivating and quickly performed. It is sensitive to small changes, not influenced by observer bias and does not have restricted scoring system as in clinical scales. The result of the assessment can be displayed on the screen in a matter of seconds. Haptic devices with properties similar to the device used in this thesis are already in use in clinics for arm rehabilitation, but to a lesser extent in assessment. In the interest of reducing the workload of clinical staff, it is imperative that technological solutions such as VR be used for training and assessment of arm function.

Recent advancements in technology have made it possible that VR-based pointing task can be designed using more sophisticated equipment and software than the methods used in this thesis. As VR technology matures with further research, VR-based tasks might become ubiquitous in clinics, where it finds application in delivering fast and accurate measurement of upper limb function after stroke. However, bringing VR-based assessment to a commercial level would need research in a larger scale, including health economics evaluation and viability studies.

It is interesting to note that the key kinematic variables emerged from this thesis reflect similar constructs as commonly perceived by persons with stroke. Individuals with stroke often describe that it takes longer time to perform daily tasks and that they feel that their arm or hand movements are less precise. Not surprisingly, movement time, velocity and smoothness were the kinematic variables that seem to be best suited to describe upper limb functioning in individuals with stroke.

Conclusions

1. Kinematic analysis is a valuable tool for assessing upper limb function after stroke. It is capable to provide information that traditional clinical scales cannot capture.
2. Movement time, mean velocity and smoothness were the kinematic variables that seem to be best suited to describe the upper limb functioning during the pointing task in individuals with stroke.
3. Kinematic variables of movement time, mean velocity and smoothness can explain only a part of variance captured by traditional clinical scales such as FMA-UE and ARAT. Thus, multi-level assessment is needed after stroke in order to understand the arm function from both clinical and kinematic perspective.
4. During the first year post-stroke, recovery of kinematic upper limb function is most evident in the acute and subacute stages of stroke, similar to that of clinical recovery. Therefore, rehabilitation interventions should focus on these stages for achieving maximum recovery of kinematic arm function. On the other hand, kinematic recovery was found to occur beyond three months after stroke, which means that continued rehabilitation is needed beyond 3 months to promote recovery and avoid decline in arm function.
5. Similar to clinical recovery, factors such as age, stroke severity at onset and type of stroke influence recovery of kinematic arm function after stroke. Thus, longer recovery times should be allowed for those with older age, more severe stroke and hemorrhagic stroke.
6. As the relationship between self-reported manual ability and objective arm function varies with time after stroke, a combination of self-reported and objective assessments should be performed in order to set achievable, patient-centric goals for arm recovery after stroke. This is more important early after stroke where there is a wide gap between self-perceived and objective assessments.

Future considerations

As technology advances with time, new assessment methods get introduced, and old ones get improvised. In future, VR-based tasks are likely to be ubiquitous and inexpensive. The knowledge gained from kinematic assessment becomes valuable in developing new devices for assessment and rehabilitation of arm function after stroke. It is hard to predict what future has in store for us, but given the technological advancements of today, it is likely that VR-based assessments have a bright future.

During the process of creating the studies included in this thesis, the following future considerations have emerged:

1. Consensus is required for choosing kinetic and kinematic measures that distinguish between different functional levels after stroke and healthy controls, that demonstrate concurrent validity with traditional clinical scales and show responsiveness to change.
2. As initial results from validating the pointing task looks promising, more research regarding its responsiveness, reliability and interpretability as well as underlying mechanisms of motor control should be investigated.
3. Relatively few studies examine kinetics, the effect of forces, on arm movement. Individuals with stroke are likely to have reduced arm strength and the measuring device is likely to exert some force on the arm, in which case it becomes important to assess the effect of forces involved in the arm movement. Measurement of kinetic variables in addition to kinematic variables would be useful to get a more complete picture of the individual’s arm function.
4. Guidelines should be established for using VR-based rehabilitation along with conventional therapy so that an optimized training strategy can be achieved. Patient selection, duration and frequency of VR-based training and nature of the task used should be closely considered before establishing guidelines for using VR-based tasks for rehabilitation.

5. Development of a simpler data handling system for kinematic analysis is warranted. This would facilitate easier data collection, analysis and interpretation.
6. There is a need for longitudinal studies using kinematic analysis in order to understand the recovery of kinematic performance after stroke. This would enable us to understand the recovery patterns in a detailed and specific way.
7. VR-based rehabilitation opens up possibilities for tele-rehabilitation. Further research should explore the use of remote assessment and rehabilitation using VR-based telerehabilitation. Similarly, robotics-supported home therapy is a new avenue that should be explored.

Acknowledgements

I express my sincere gratitude to all the participants involved in this study, who, despite their disability or tight schedule consented to spend a significant amount of time for providing us the information we need for performing our studies. I am humbled by their determination and perseverance. Many of the participants were motivated by the idea of playing their part in helping us to push the boundaries of science. I hope to do justice to their mission and to their cause.

The Sahlgrenska Academy of University of Gothenburg took care of everything for me so that I could lay complete focus in research. I didn't have to worry about resources, because they were made available in plenty at all times. The Academy provided me with opportunities not only for developing me as a researcher, but also as a well-rounded person. I shall forever be grateful.

I got the privilege to have Katharina S. Sunnerhagen as my main supervisor during the first half of my PhD. Katharina's hardwork and passion for research never ceased to amaze me. She often went the extra mile to review my work, even during off-hours and vacation days. Her wisdom and generosity were the key factors that kept me moving forward when I met with obstacles during the course of my PhD. The multiprofessional, multicultural and inspiring research group which I am a part of was made possible by Katharina's vision and dedication. Thank you, Katharina, for believing in me, and for helping me to grow to my full potential. With you by my side, I did things I once never dreamt of doing.

I am extremely lucky to have Margit Alt Murphy as my main supervisor during the second half of my PhD. She listened to all my ideas, refined them, asked intriguing questions and reviewed my drafts with extreme patience. She was always open for discussion during which she made sure to spark my curiosity and raise my enthusiasm. Margit's extensive knowledge and attention to detail were crucial in developing this thesis to its current form. Thank you, Margit, for constantly striving to bring out the best in me.

I am grateful to Åsa Lundgren-Nilsson, my co-supervisor, for sharing her expertise and experience with me. Despite her busy schedule, Åsa ensured that she spent quality time with me. She helped me to see through many aspects of the project which I would not have seen for myself. I have benefitted greatly from her straightforward approach to problem solving. Thank you, Åsa, for your support and guidance.

I am thankful to all my colleagues at Rehabilitation Medicine Research Group. You stood by me at all times and made my transition to Sweden smooth and pleasant. The discussions we had about science, research and life in general were enlightening and informative. I extend my gratitude especially to Karin Törnbom, Lena Rafsten, Emma Kjörk, Ulrica Jonsson, Tamar Abzhandadze, Lamprini Lili, Eva Lena Bustrén, Emma Westerlind, Dongni Johansson, Hanna Persson, Malin Reinholdsson, Sofi Andersson, Annie Palstam, Anna Dencker, Anna Danielsson, Elisabeth Brodin, Elisabeth Åkerlund, Ann Björkdahl, Adam Viktorisson, David Krabbe, the researchers, students, interns and staff of Rehabmedicin for your cordial friendship, discussions and encouragement.

Jurgen Broeren began researching on the pointing task using VR as early as in 2002. My work is, in effect, a continuation of his research. Daniel Goude's work on Curictus software made it possible for me to capture kinematic data from the pointing task. Thank you, Jurgen and Daniel for laying the grounds on which this thesis is built on.

I got the opportunity to observe at the stroke unit of Sahlgrenska Universitietssjukhuset, where I met patients and caretakers. This experience helped me to learn about stroke from the clinical perspective. I am thankful to specialist doctors Jan-Erik Karlsson and Petra Redfors for overseeing me during my observership.

My life partner Anver Hisham supported me both personally and professionally. He helped sometimes by suggesting ideas, sometimes by writing code and sometimes by just listening me out patiently. A PhD himself, Anver's foresight was crucial for developing my perspectives about research, interdisciplinarity and career. The MATLAB library that he created for organizing my data helped me save a lot of time and effort. Thank you, Anver, for all the wisdom, fun and the hugs.

Sweden offered me a generous welfare system, beautiful nature and immense hospitality. The landscape, flora and fauna around Härlanda offered me solitude and tranquility. I made good use of the extensive collection of books at libraries across Sweden which helped me shape my perspectives. I am fortunate to have lived here over the last four years.

My work has also been influenced by many mentors, colleagues and friends. I am thankful to my friends at the Wikimedia movement, Chalmers University of Technology, TED, Infoclinic, Keralites in Göteborg, Svenska som andraspråk, Mozilla and Internationella Läkareföreningen i Sverige (ILF) for their companionship and fruitful discussions. From you, I found ideas worth pursuing and principles worth championing for.

My parents Juvairia and Hussain E.M were a constant source of support and encouragement. They played an important role in making me the person I am today. My sister Fidha Hussain was always there for me, lending me an empathic ear whenever I needed it. I relied on her uncanny knack for seeing the lighter side of things when difficult situations arose. My parents-in-law Soudha and Siddique believed in me and whole-heartedly supported everything I did. My extended family living in Kerala and the Middle East were excited by the prospects of me pursuing a PhD, and offered a lot of love from afar. Thank you all for your endless amounts of love and inspiration.

ആശതീർന്നാൽ സമ്പത്തായി/A contented mind is a continual feast

Summary in Malayalam

തലച്ചോറിലേക്കുള്ള രക്തചംക്രമണത്തിന് തടസ്സം നേരിടുമ്പോൾ വരുന്ന അവസ്ഥയെയാണ് സ്ട്രോക്ക് അഥവാ മസ്തിഷ്കാഘാതം എന്ന് വിളിക്കുന്നത്. ലോകാരോഗ്യ സംഘടനയുടെ നിർവ്വചനപ്രകാരം രക്തചംക്രമണവ്യവസ്ഥയിൽ ഉത്ഭവിക്കുന്നതും, 24 മണിക്കൂറിലധികം നീണ്ടുനിൽക്കുകയോ മരണത്തിൽ കലാശിക്കുകയോ ചെയ്യുന്നതുമായ മസ്തിഷ്കത്തിലെ കേന്ദ്രീകൃതമോ, വ്യാപകമോ ആയ പ്രവർത്തനക്ഷയത്തെയാണ് സ്ട്രോക്ക് എന്ന് വിളിക്കുന്നത്. സ്ട്രോക്ക് മൂലം കൈകാലുകളിൽ ബലക്ഷയം, സ്പർശനശേഷിക്കുറവ്, ഓർമ്മക്കുറവ്, സംസാരശേഷിക്കുറവ് എന്നിങ്ങനെ വിവിധ രോഗലക്ഷണങ്ങൾ ഉണ്ടാവുകയും, തൽഫലമായി ദൈനംദിന പ്രവർത്തികളിൽ ഏർപ്പെടാൻ ബുദ്ധിമുട്ട് അനുഭവപ്പെടുകയും ചെയ്തേക്കാം. ലോകമെമ്പാടും 2.5 കോടി ജനങ്ങളാണ് സ്ട്രോക്കിനു ശേഷമുള്ള പ്രത്യാഘാതങ്ങളുമായി ജീവിക്കുന്നത്. ഇത്രയധികം വ്യക്തികളുടെ ദൈനംദിനജീവിതത്തെ ബാധിക്കുന്ന രോഗമാണ് സ്ട്രോക്ക് എന്നതുകൊണ്ട് ഈ അവസ്ഥയിൽ നിന്നും അവരെ സുഖപ്പെടുത്തേണ്ടതിനും, അവരെ സാധാരണ ജീവിതം നയിക്കാൻ പ്രാപ്തമാക്കേണ്ടതിനുമുള്ള ഗവേഷണങ്ങൾ നടത്തുന്നതിന് ശാസ്ത്രസമൂഹം കൂടുതൽ പരിഗണന നൽകേണ്ടതുണ്ട്.

സ്ട്രോക്കിനു ശേഷം കൈകൾക്ക് ബലക്ഷയം വന്നിട്ടുള്ളവരുടെ കൈകളുടെ പ്രവർത്തനനില അളക്കാനുള്ള ഒരു നൂതന സാങ്കേതികവിദ്യയാണ് ഈ ശാസ്ത്രപ്രബന്ധത്തിൽ പരിചയപ്പെടുത്തുന്നത്. ത്രീ-ഡി സിനിമകളിലും മറ്റും ഉപയോഗിക്കുന്ന വിർച്ചൽ റിയാലിറ്റി എന്ന സാങ്കേതികവിദ്യ ഉപയോഗിച്ച് നിർമ്മിച്ച ഒരു ലളിതമായ കമ്പ്യൂട്ടർ ഗെയിം ആണ് ഈ പുസ്തകത്തിൽ പരിചയപ്പെടുത്തുന്നത്. ത്രീഡി കണ്ണടകളും കമ്പ്യൂട്ടറും ഉപയോഗിച്ച് ത്രിമാനമായ വസ്തുക്കൾ കാണുന്ന പ്രതീതി ഉണ്ടാക്കിയെടുക്കാൻ കഴിയുന്ന സാങ്കേതിക വിദ്യയെയാണ് വിർച്ചൽ റിയാലിറ്റി എന്ന് വിളിക്കുന്നത്. ഈ കമ്പ്യൂട്ടർ ഗെയിമിൽ, ത്രീഡി കണ്ണട ധരിച്ച വ്യക്തി പേന പോലുള്ള ഒരു ഉപകരണം ഉപയോഗിച്ച്, ത്രിമാന ഗോളങ്ങളെ തൊട്ട് അപ്രത്യക്ഷമാക്കുന്നു. എത്രയും പെട്ടെന്ന് എല്ലാ ഗോളങ്ങളെയും തൊട്ട് അപ്രത്യക്ഷമാക്കുക എന്നതാണ് ഗെയിമിൻ്റെ ലക്ഷ്യം. ഗെയിമിനിടയിൽ വ്യക്തി കൈ കൊണ്ട് നടത്തുന്ന എല്ലാ ചലനങ്ങളും കമ്പ്യൂട്ടറിൽ രേഖപ്പെടുത്തുന്നു. ഈ ചലനങ്ങൾ അടങ്ങുന്ന ഡേറ്റ വിഗ്രഹിച്ച്, ചലനചരങ്ങൾ (kinematic variables) എന്ന ഗണിത പരിമാണങ്ങൾ കണക്കുകൂട്ടുന്നു. ചലനചരങ്ങൾ ഉപയോഗിച്ച് സ്ട്രോക്ക് ഉള്ളവരുടെ കൈകളുടെ ചലനത്തെക്കുറിച്ച് വിശദമായി പഠിക്കാവുന്നതാണ്. ഈ പ്രബന്ധം തയ്യാറാക്കാനായി 67 സ്ട്രോക്ക് ഉള്ള വ്യക്തികളെയും, 43 ആരോഗ്യമുള്ള വ്യക്തികളെയുമാണ് പഠനത്തിനു വിധേയരാക്കിയത്.

ഈ പ്രബന്ധത്തിൽ നാല് പഠനങ്ങളാണ് ഉൾക്കൊള്ളിച്ചിരിക്കുന്നത്. ഒന്നാമത്തെ പഠനത്തിൽ, സ്ട്രോക്ക് ബാധിച്ച വ്യക്തികളുടേയും, ആരോഗ്യമുള്ള വ്യക്തികളുടെയും

കൈകളുടെ ചലനങ്ങളിൽ ഉള്ള വ്യത്യാസങ്ങൾ ആണ് പഠനത്തിന് വിധേയമാക്കിയത്. കൈകളുടെ ചലനസമയം, ചലനവേഗം, മൂർദ്ധന്യവേഗം, ചലനത്തിനുള്ള ആയാസം എന്നീ ചലനചരങ്ങൾ സ്ട്രോക്ക് ബാധിച്ച വ്യക്തികളിലും ആരോഗ്യമുള്ളവരിലും ഏതെല്ലാം തരത്തിൽ വ്യത്യസ്ഥപ്പെട്ടിരിക്കുന്നു എന്ന് ഈ പഠനത്തിലൂടെ കണ്ടെത്തി. സ്ട്രോക്ക് ബാധിച്ച വ്യക്തികളുടെ ചലനങ്ങൾ അളക്കുന്നതിനും, രോഗികളുടെ ചികിത്സ നിർണ്ണയിക്കുന്നതിനും ഈ പഠനഫലം ഉപയോഗയോഗ്യമാണ്.

കൈകളുടെ ശേഷി അളക്കാൻ ഉപയോഗിക്കുന്ന ക്ലിനിക്കൽ പരിശോധനകളും ചലനചരങ്ങളും തമ്മിലുള്ള ബന്ധമാണ് രണ്ടാമത്തെ പഠനത്തിൽ ഉൾക്കൊള്ളിച്ചിരിക്കുന്നത്. സ്ട്രോക്ക് ഉള്ള വ്യക്തികളുടെ കൈകളുടെ ചലനങ്ങൾ നിരീക്ഷിച്ച് രേഖപ്പെടുത്താൻ ക്ലിനിക്കുകളിൽ സാധാരണയായി ഉപയോഗിക്കുന്ന രണ്ട് പരിശോധനകൾ ആണ് ഫ്യൂഗൽ-മേയർ മാനകവും (Fugl-Meyer Assessment of Upper Extremity), ആക്ഷൻ റിസർച്ച് ആം ടെസ്റ്റ് (Action Research Arm Test) എന്ന മാനകവും. ഫ്യൂഗൽ മേയർ മാനകത്തിനും ചലനചരങ്ങൾക്കും 16% സാമ്യത ഉണ്ട് എന്ന് ഈ പഠനത്തിലൂടെ കണ്ടെത്തി. ആക്ഷൻ റിസർച്ച് ആം ടെസ്റ്റിനാകട്ടെ, 13% ആണ് ചലനചരങ്ങളുമായി സാമ്യത ഉള്ളത്. ക്ലിനിക്കൽ പരിശോധനകൾക്ക് കൃത്യമായി അളക്കാനാവാത്ത കൈകളുടെ സ്വഭാവവിശേഷതകൾ ആണ് ചലനചരങ്ങൾ അളക്കുന്നത് എന്നാണ് ഈ ഗവേഷണഫലത്തിൽ നിന്നും മനസിലാക്കാവുന്നത്. അതിനാൽ, സ്ട്രോക്ക് ബാധിച്ച വ്യക്തികൾക്ക് ക്ലിനിക്കൽ പരിശോധനകൾ ചെയ്യുന്നതിനോടൊപ്പം ചലനചരങ്ങൾ കൂടി അളക്കുന്നതിലൂടെയേ അവരുടെ അംഗപരിമിതത്വത്തെക്കുറിച്ച് പൂർണ്ണമായ ചിത്രം കിട്ടുകയുള്ളൂ.

മൂന്നാമത്തെ പഠനത്തിൽ, സ്ട്രോക്ക് ബാധിച്ച വ്യക്തികളുടെ കൈകളുടെ പ്രവർത്തനം ആദ്യ ഒരു വർഷത്തിനുള്ളിൽ എപ്രകാരം മെച്ചപ്പെടുന്നു എന്നതാണ് ചലനചരങ്ങൾ ഉപയോഗിച്ച് പഠനവിധേയമാക്കിയിട്ടുള്ളത്. ചലനസമയം, ചലനവേഗം, ചലനത്തിനുള്ള ആയാസം എന്നീ ചലനചരങ്ങൾ സ്ട്രോക്കിന് ശേഷം ഒരു വർഷത്തിനുള്ളിൽ മെച്ചപ്പെട്ട് വരുന്നു എന്നത് ഈ പഠനത്തിലൂടെ മനസിലാക്കി. കുറഞ്ഞ പ്രായം ഉള്ളവരും, തീവ്രമല്ലാത്ത സ്ട്രോക്ക് ബാധിച്ചവരും, രക്തചംക്രമണക്കുറവ് മൂലം സ്ട്രോക്ക് ബാധിച്ചവരും മറ്റുള്ളവരെക്കാൾ വേഗത്തിൽ കൈകളുടെ ചലനങ്ങളിൽ പുരോഗതി നേടുന്നു എന്നതും ഈ പഠനത്തിലൂടെ മനസിലാക്കി. സ്ട്രോക്ക് വന്നതിനു മൂന്ന് മാസത്തിനു ശേഷവും ചലനചരങ്ങളിൽ ചെറിയ പുരോഗതി ഉണ്ടാവുന്നതായും കണ്ടെത്തി. സ്ട്രോക്ക് വന്നതിനു ശേഷം ആറാമത്തെ മാസത്തെ ചലനചരങ്ങൾ ആരോഗ്യമുള്ള വ്യക്തികളുടേതുമായി താരതമ്യം ചെയ്തപ്പോൾ രണ്ടും തമ്മിൽ പ്രബലമായ വ്യത്യാസങ്ങൾ ഇല്ലെന്നും കണ്ടെത്തി.

സ്ട്രോക്ക് ബാധിച്ച വ്യക്തികൾ സ്വയം മനസിലാക്കുന്ന കൈകളുടെ അംഗപരിമിതിയും, ചലനചരങ്ങൾ ഉപയോഗിച്ച് കണക്കാക്കിയ

അംഗപരിമിതിയും തമ്മിലുള്ള ബന്ധമാണ് നാലാമത്തെ പഠനത്തിൽ പഠനവിധേയമാക്കിയിട്ടുള്ളത്. സ്ട്രോക്ക് വന്ന് ആദ്യത്തെ ആഴ്ചകളിൽ വ്യക്തിക്ക് തങ്ങളുടെ കൈകളുടെ ചലനക്ഷമതയെക്കുറിച്ച് കുറഞ്ഞ ധാരണയേ ഉള്ളൂ എന്നും, എന്നാൽ ഏതാനും മാസങ്ങൾക്ക് ശേഷം തങ്ങളുടെ ചലനക്ഷമതയെക്കുറിച്ച് അവർ കൂടുതലായി ബോധവാന്മാരാകുന്നുണ്ട് എന്നും പഠനത്തിലൂടെ കണ്ടെത്തി. സ്ട്രോക്ക് ബാധിച്ച വ്യക്തി സ്വയം നിർണ്ണയിച്ച ചലനക്ഷമതയും ചലനചരങ്ങൾ ഉപയോഗിച്ച് നിർണ്ണയിച്ച ചലനക്ഷമതയും തമ്മിൽ വ്യത്യാസങ്ങൾ ഉണ്ട് എന്ന വസ്തുതയെക്കുറിച്ച് ചികിത്സകരും രോഗികളും ബോധവാന്മാരായിരിക്കേണ്ടതുണ്ട്. സ്ട്രോക്ക് ബാധിച്ച വ്യക്തിയുടെ മികച്ച പുനരധിവാസം സാധ്യമാക്കണമെങ്കിൽ തങ്ങളുടെ ചലനക്ഷമതയെയും പരിമിതികളെയും കുറിച്ചുള്ള കൃത്യമായ കാഴ്ചപ്പാട് അവർക്ക് നൽകേണ്ടതുണ്ട്.

It is hard to indeed notice anything for which the languages available to us have no description.

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